« il était question d’un Voyage »

ECN

- Items 1, 2, 181, 198, 267, 279, 319

Victoria BLARY, Laetitia BASTIDE, Sophie ARTRU, Nicolas **MATHIEU**

Hepato-gastroenterology and digestive oncology department,

University Hospital, F-38000 Grenoble, France

VOYAGE AU CŒUR DES MÉCANISMES D'ACTION DES TRAITEMENTS DES MICI

Liens d’intérêts : Nicolas Mathieu

Au cours des 3 dernières années,
avec les sociétés Pharmaceutiques suivantes

Recherches cliniques : AMGEN, GILEAD, PAREXEL

Advisory Boards : ABBVIE, FERRING, JANSSEN

Cours, formations : ABBVIE, FERRING, MSD, MEDTRONICS, PFIZER, TAKEDA

Aides pour des recherches : ABBVIE, FERRING, MEDTRONICS, PFIZER, TAKEDA

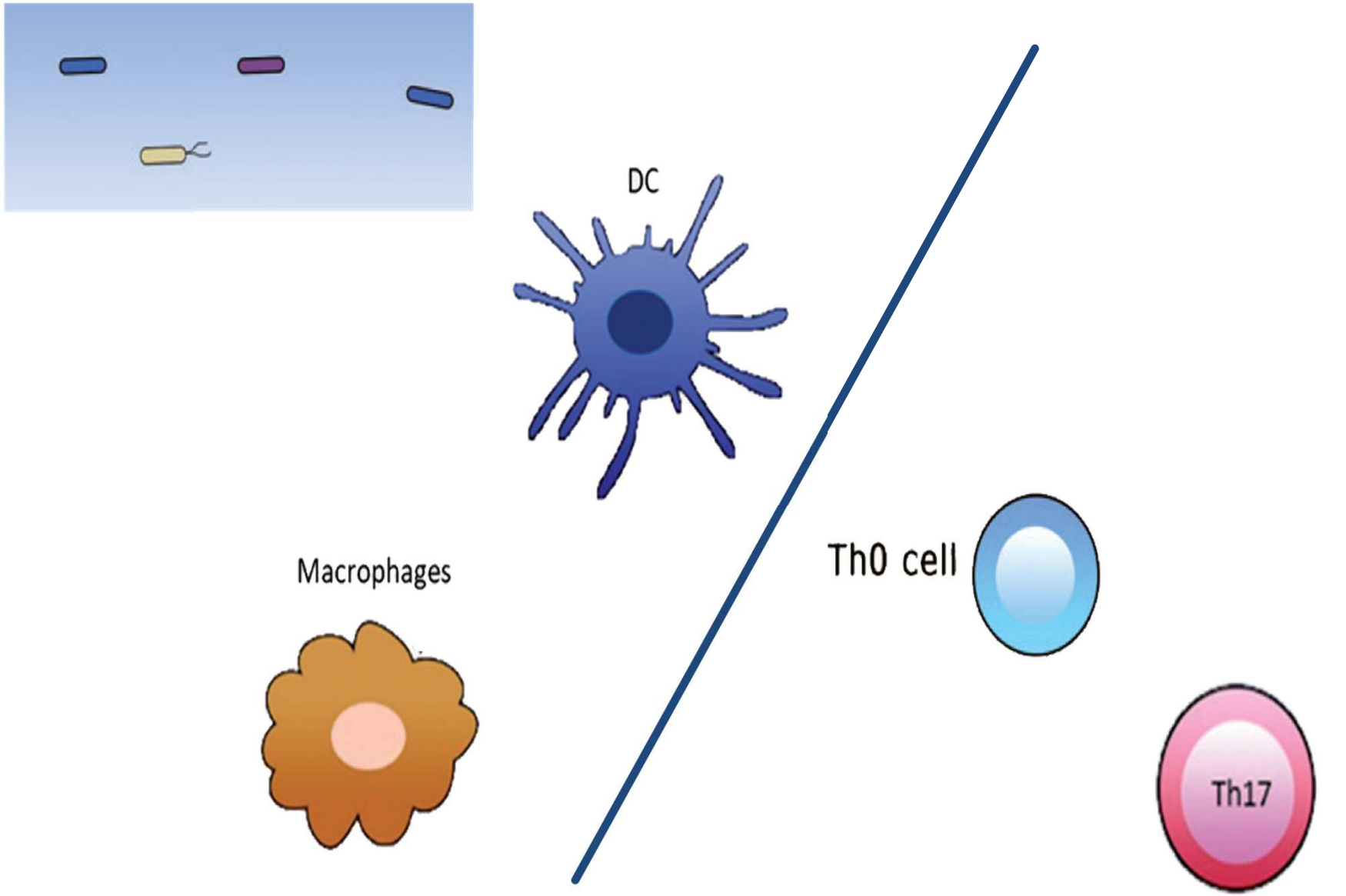
Veronese, Banquete na Casa de Levi, 1573

Nicolas **MATHIEU**

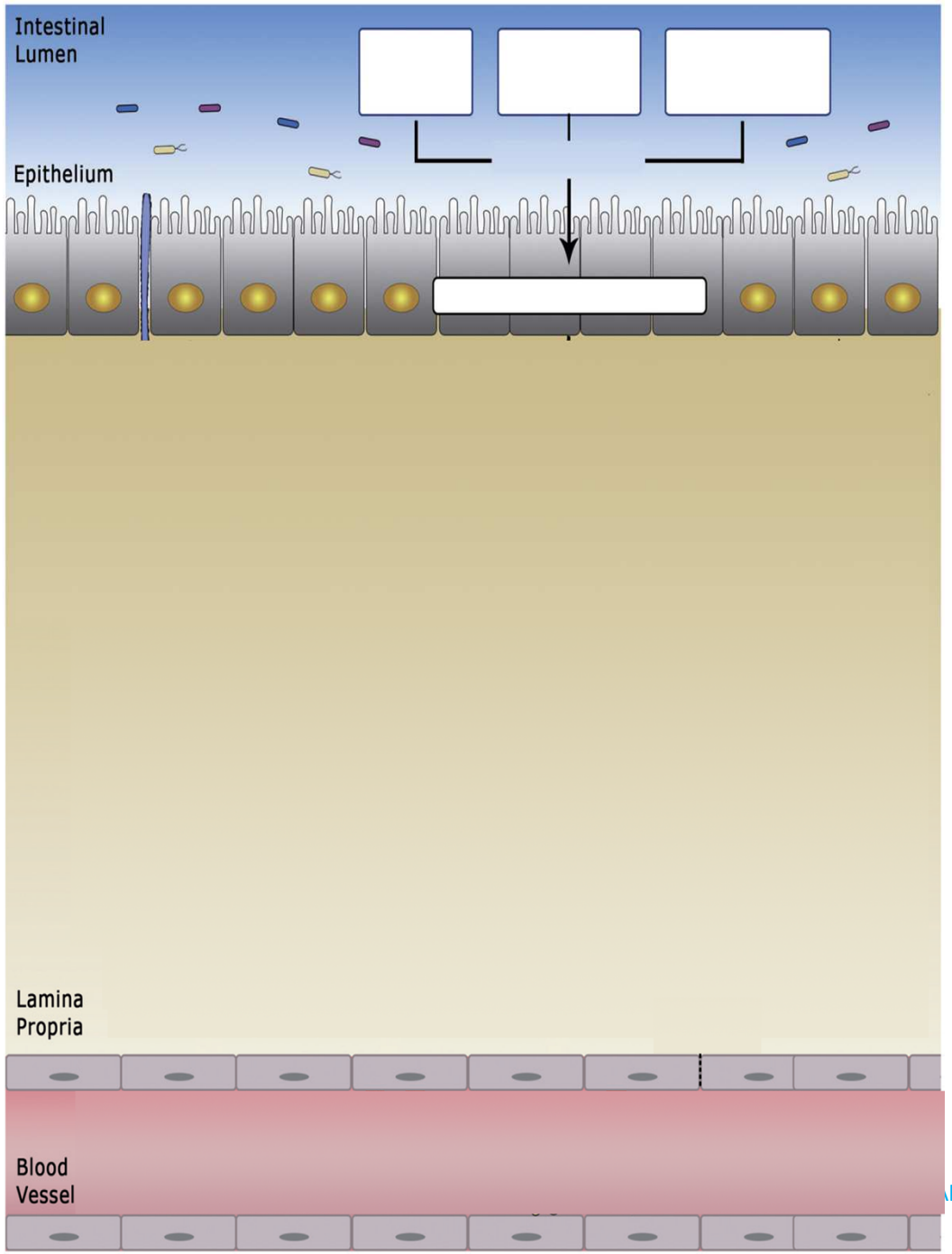
LE VOYAGE FANTASTIQUE

Que le Grand Anaconda Immuno daigne me Pardonner

JE VAIS ÊTRE SCHÉMATIQUE…



Ahluwalia A *et al. Scand J Gactroenterol.* 2018;53:379-389.



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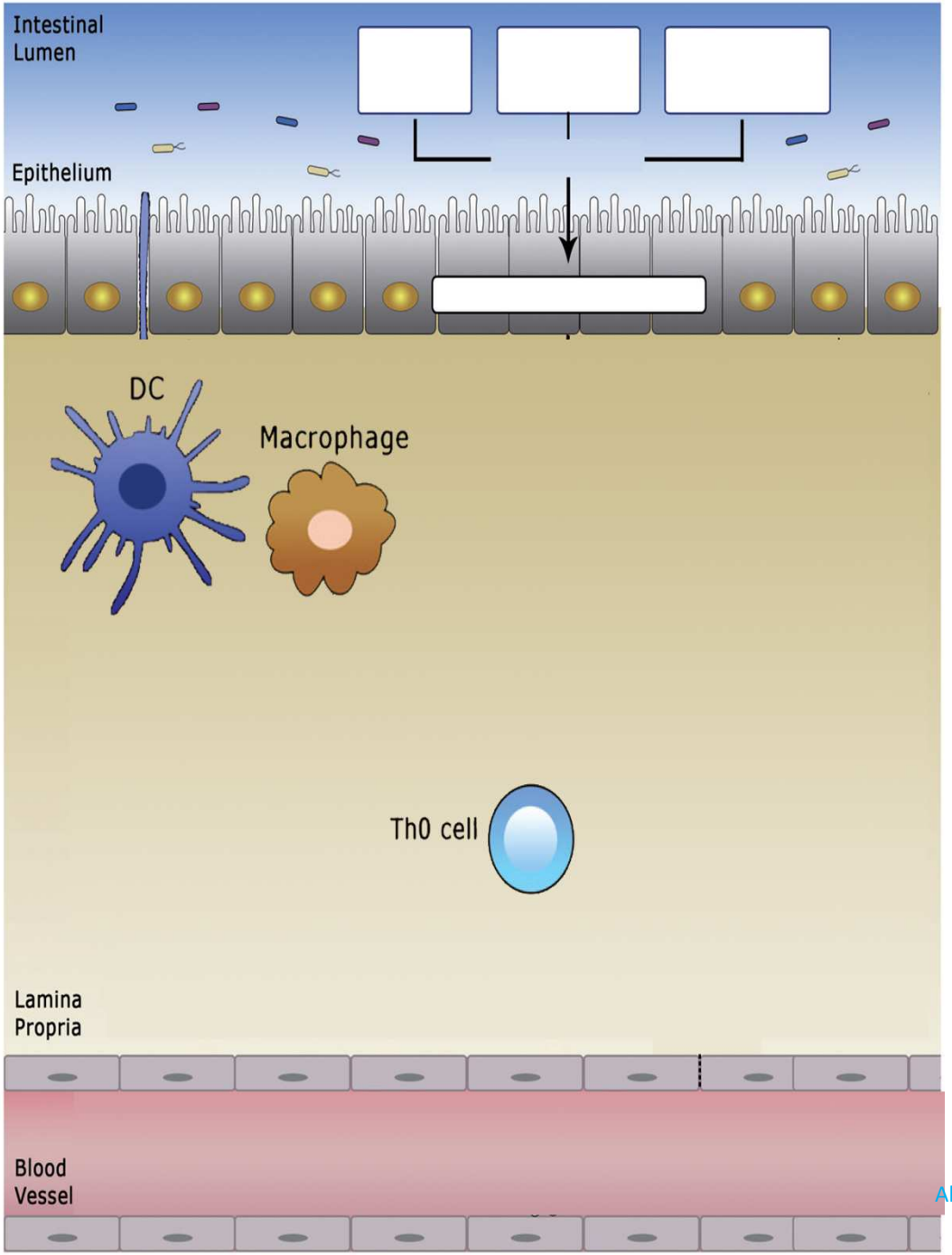
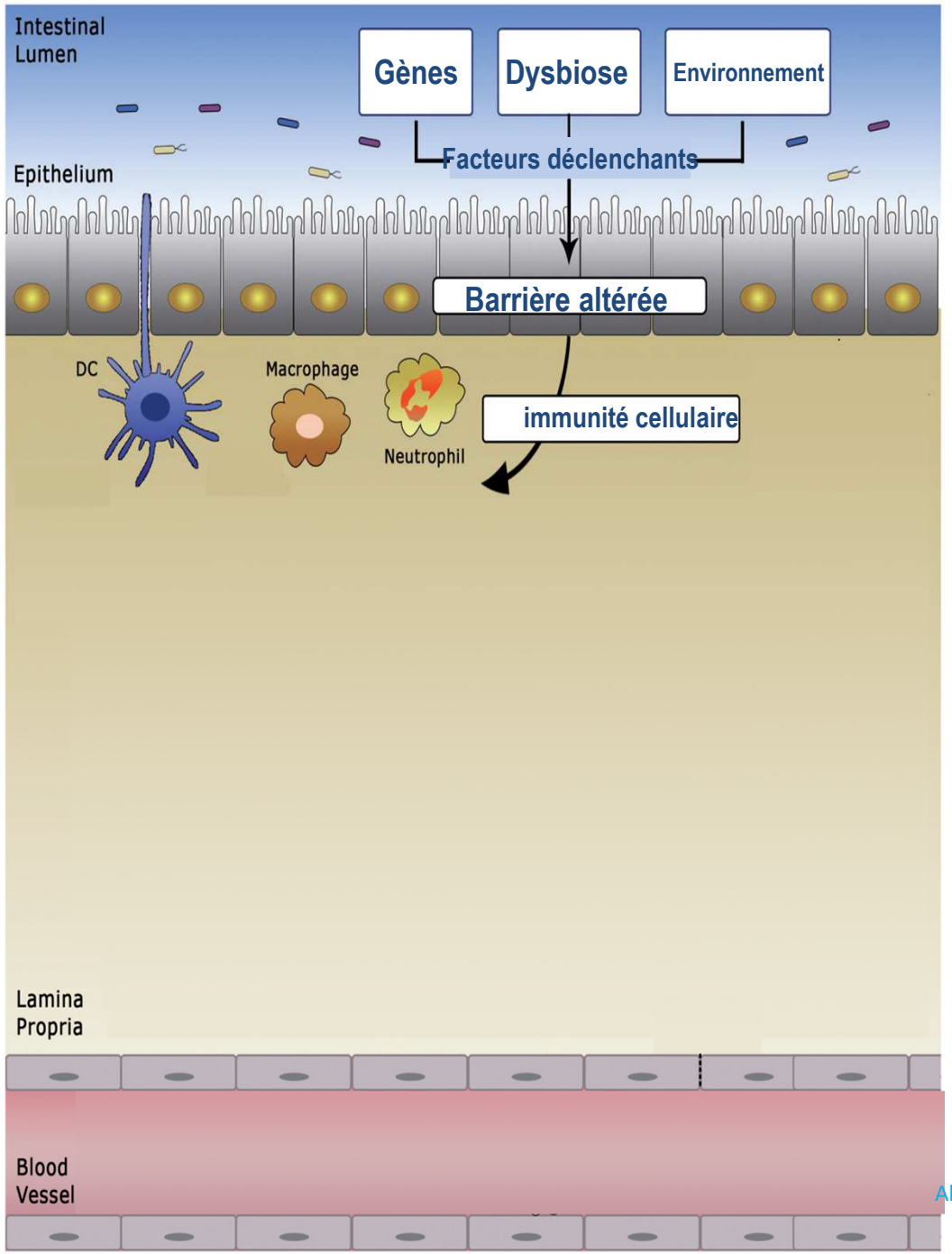
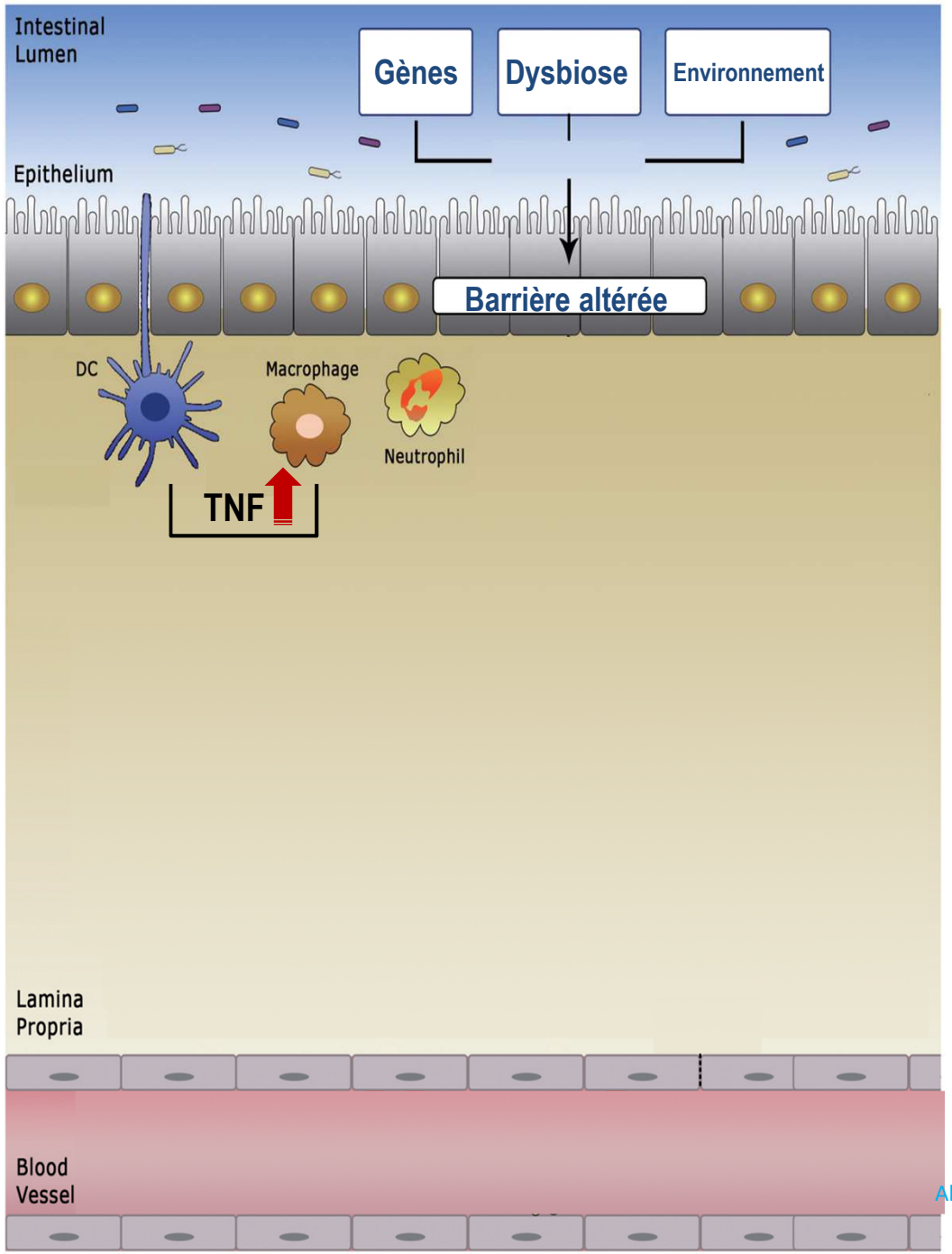


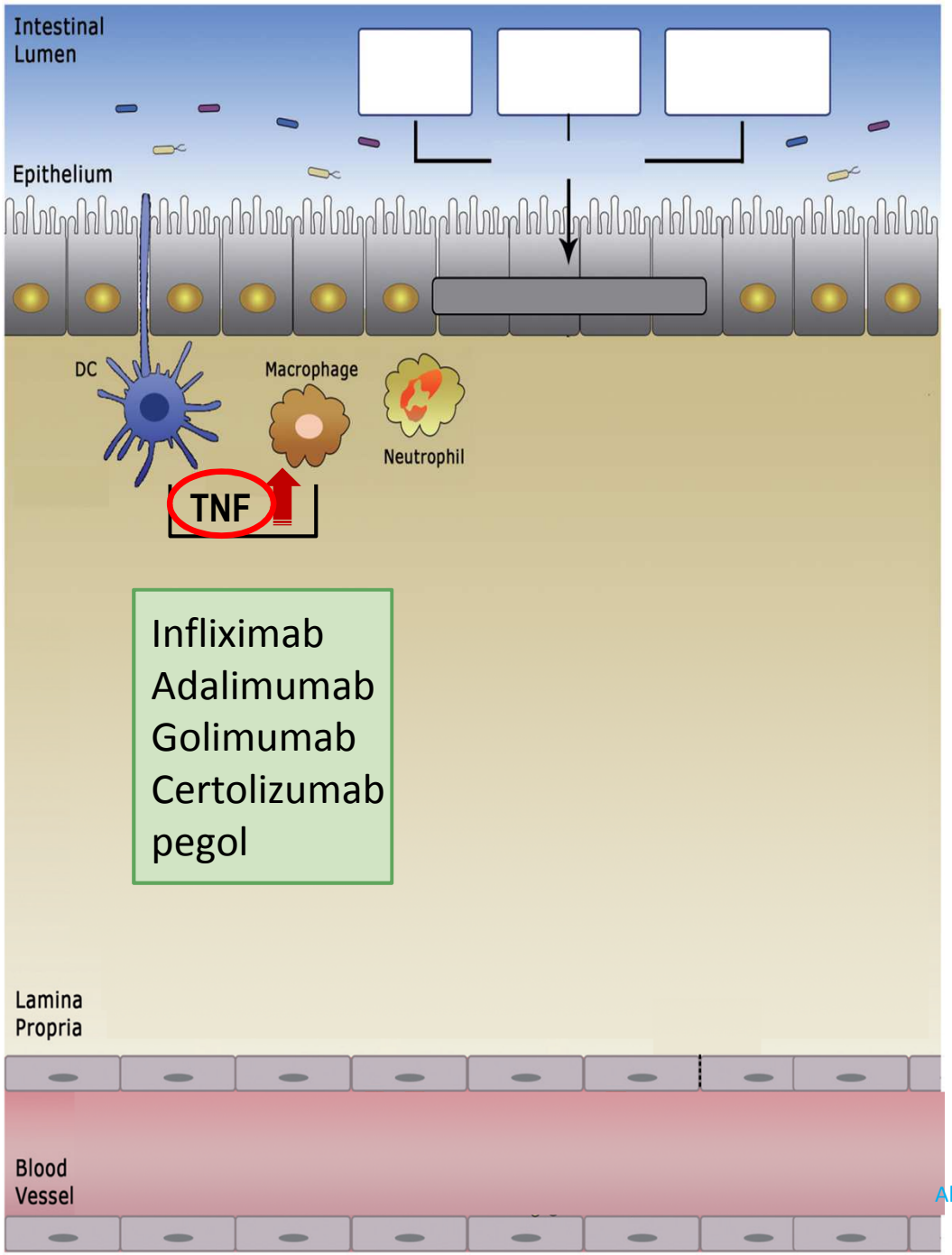
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



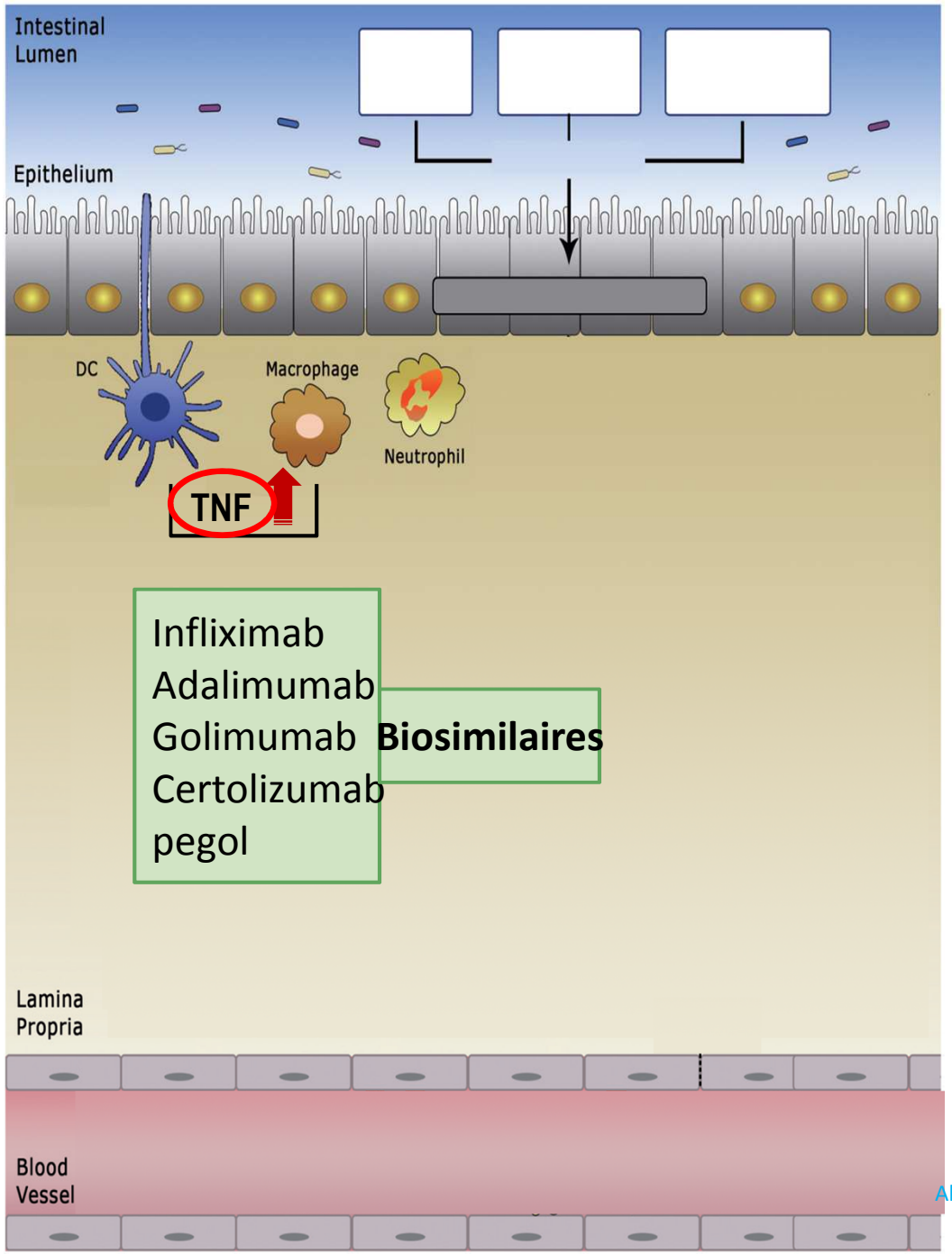
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



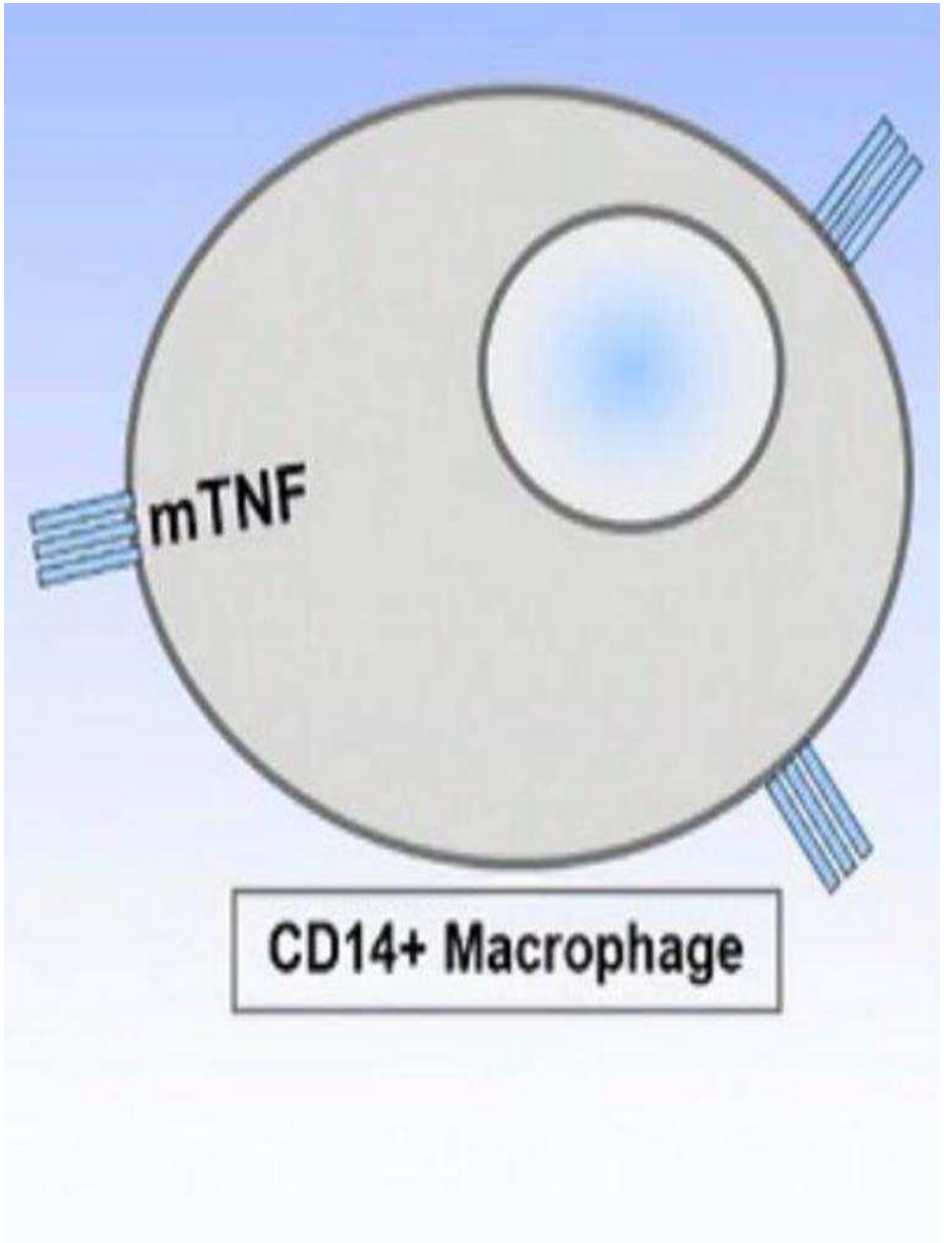
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

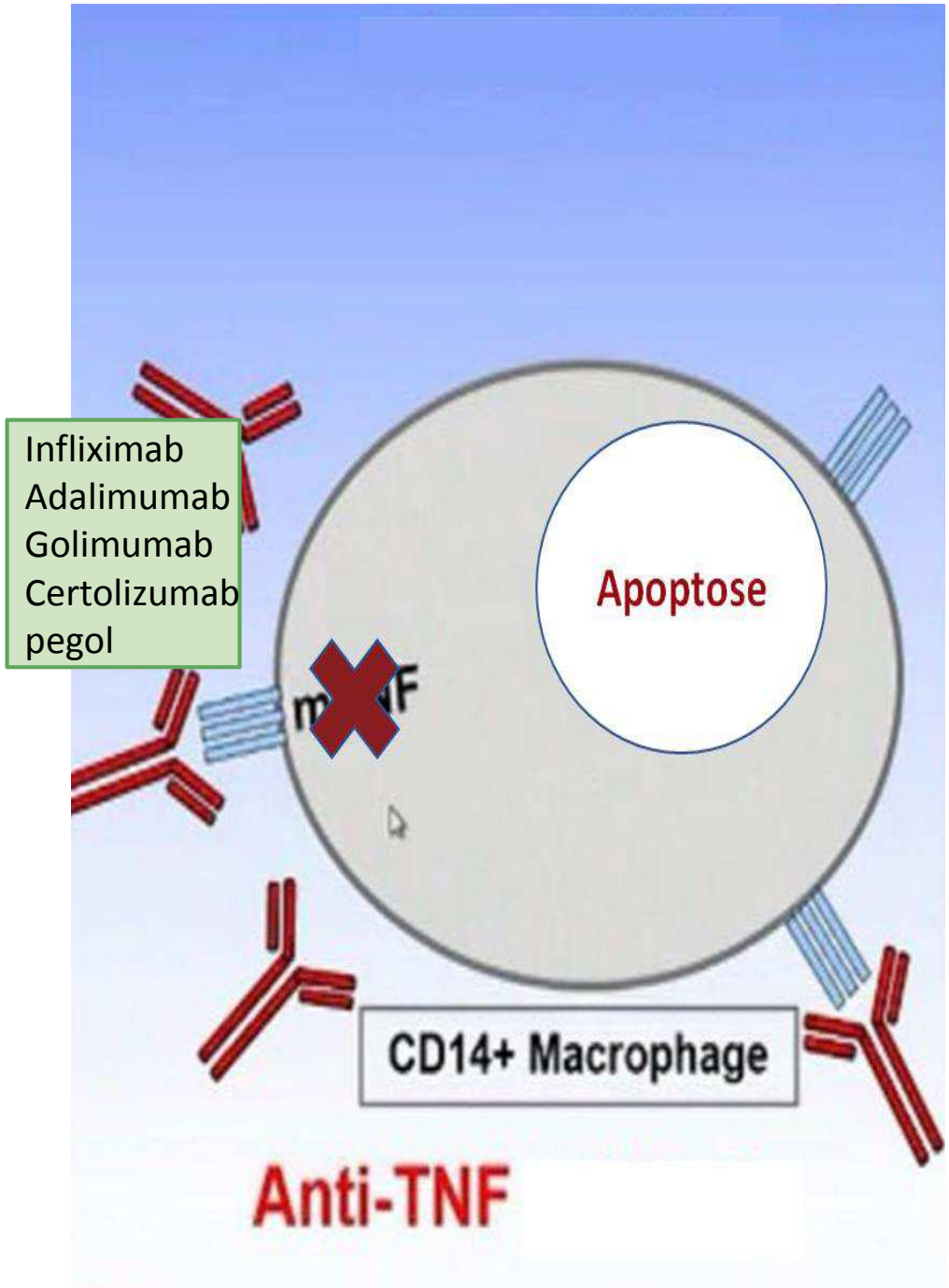


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



Infliximab
Adalimumab
Golimumab
Certolizumab pegol

Ten Hove T *et al. Gut* 2002; 50:206-11
Di Sabatino A *et al. Gut* 2004; 53:70-77
Levin AD *et al. ECCOJC* 2016; 10:989-997



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Sabatino A *et al. Gut* 2004; 53:70-77
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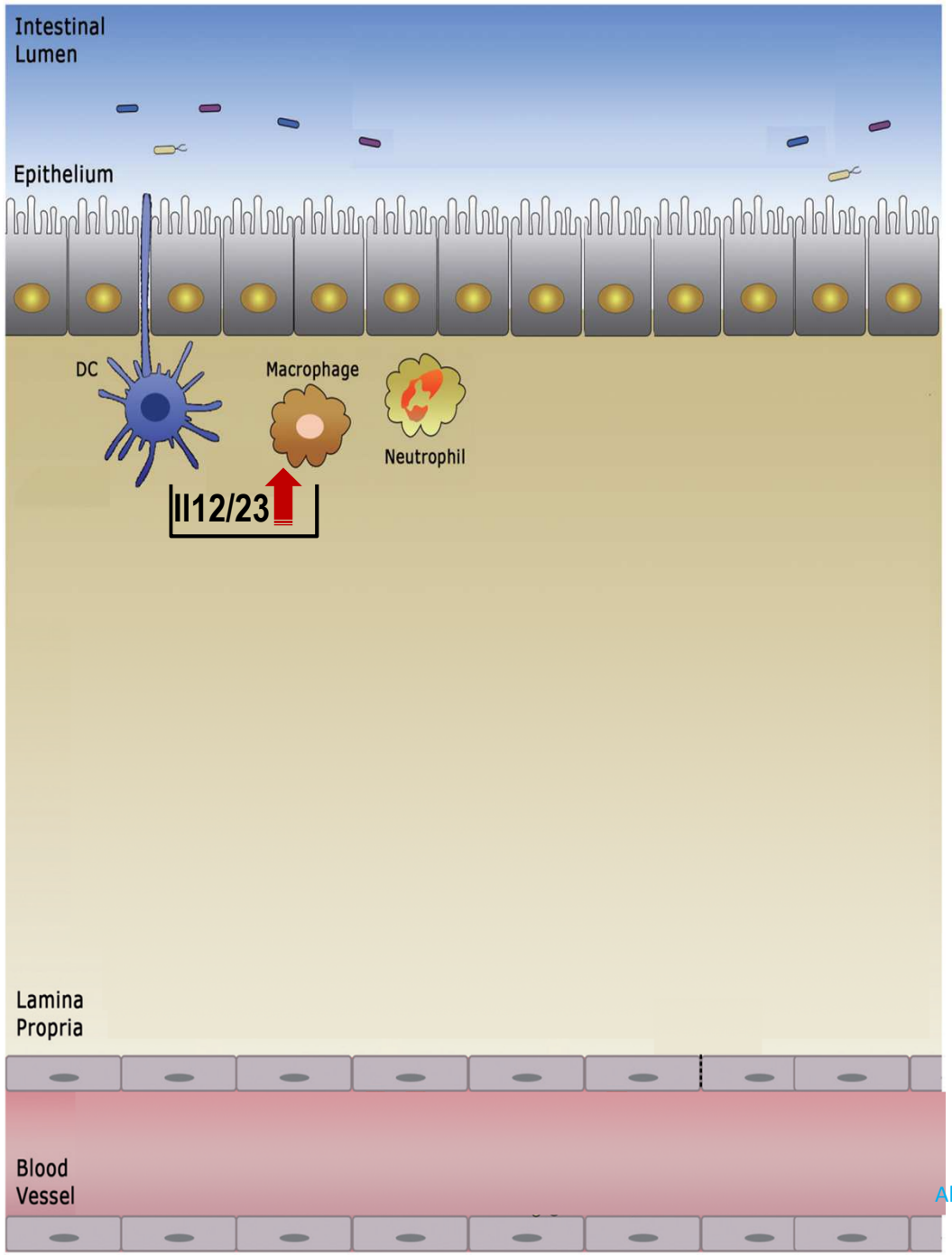

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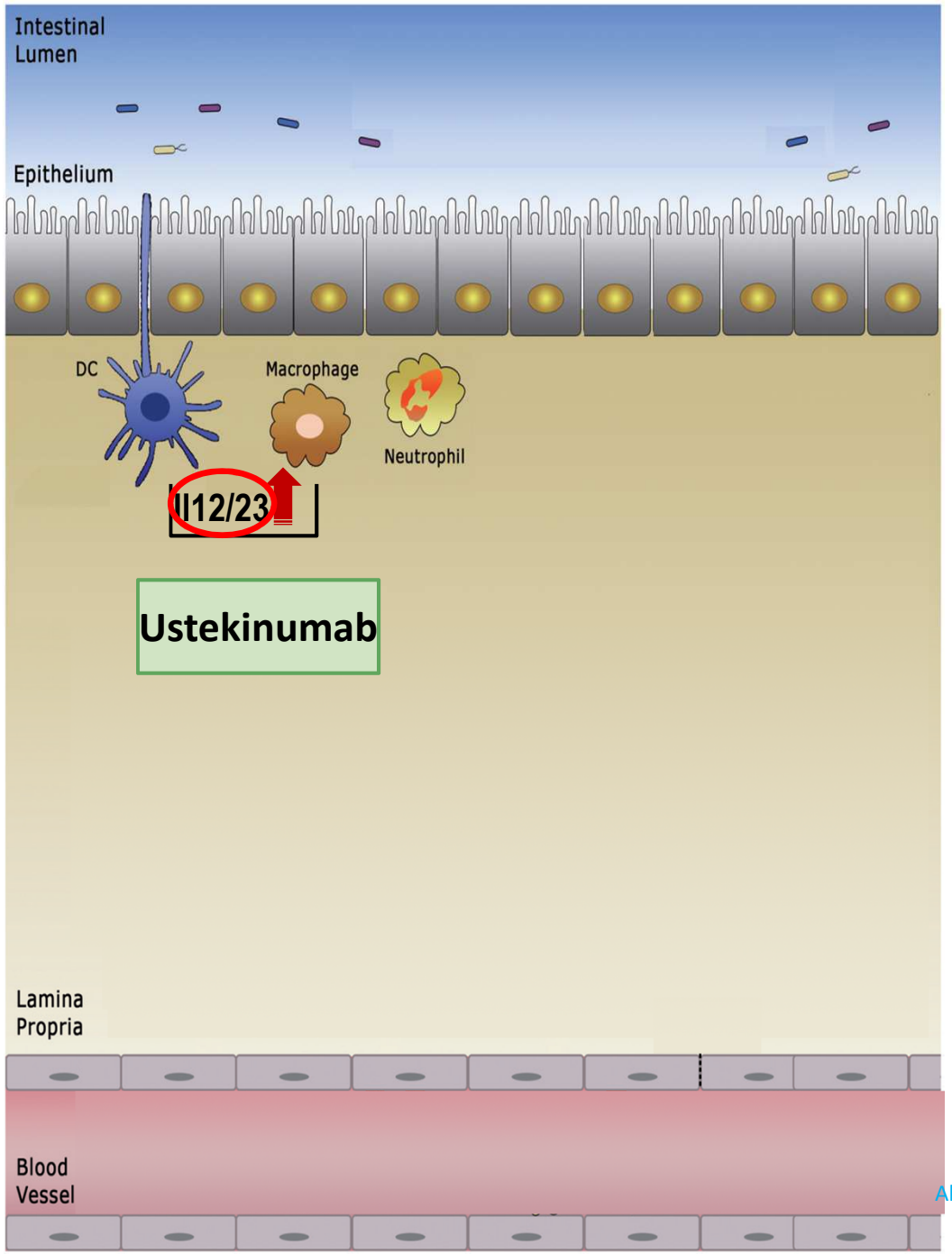
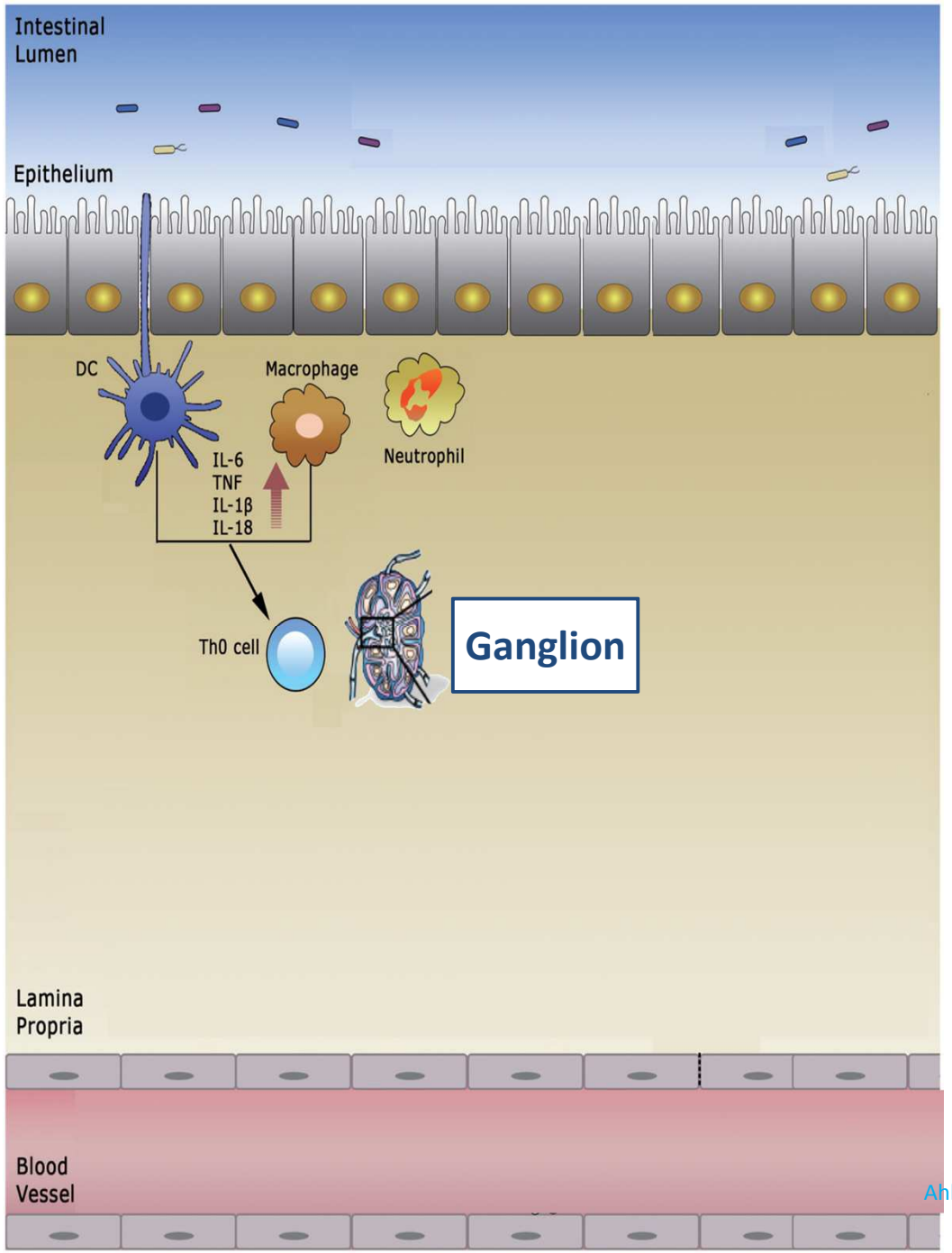
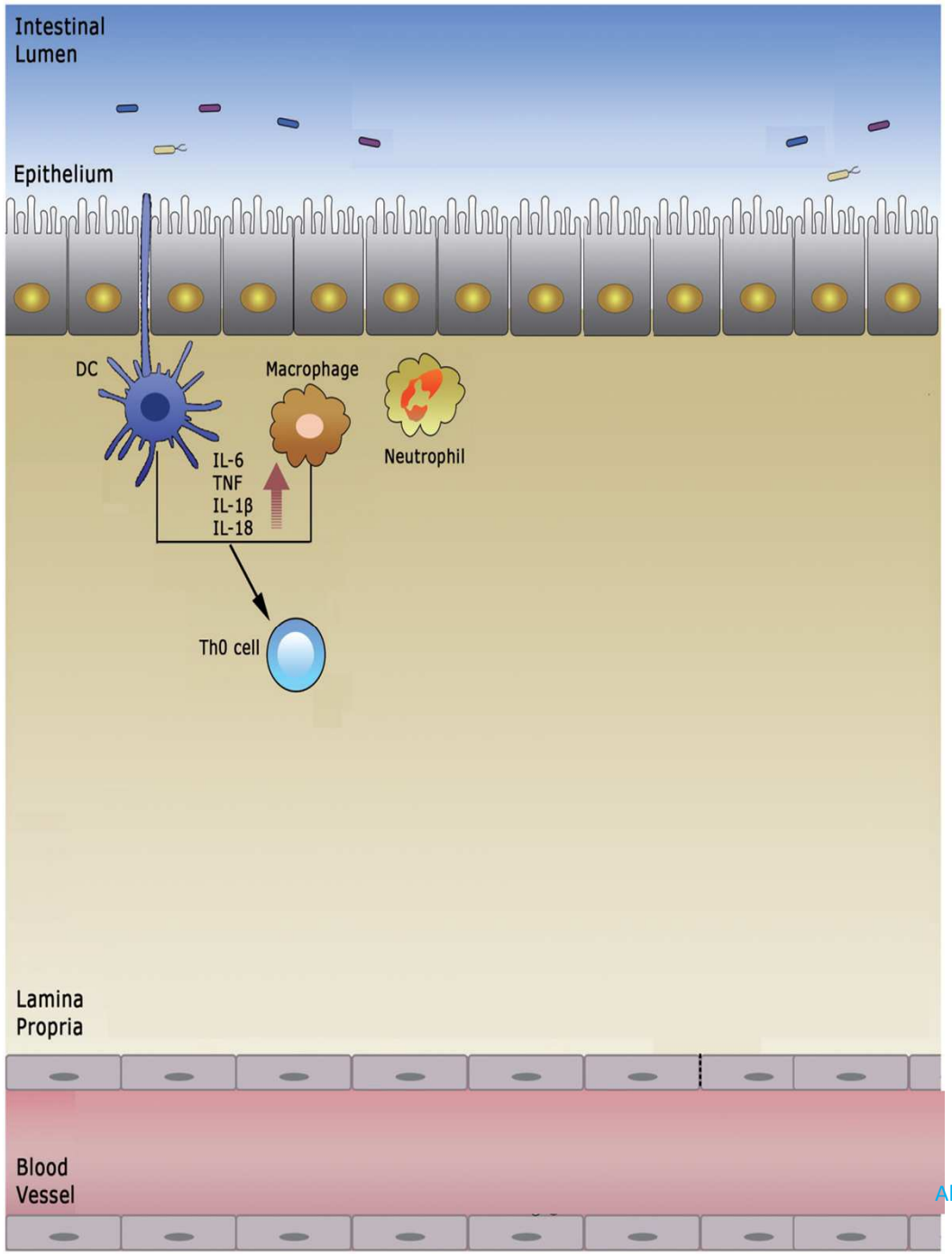


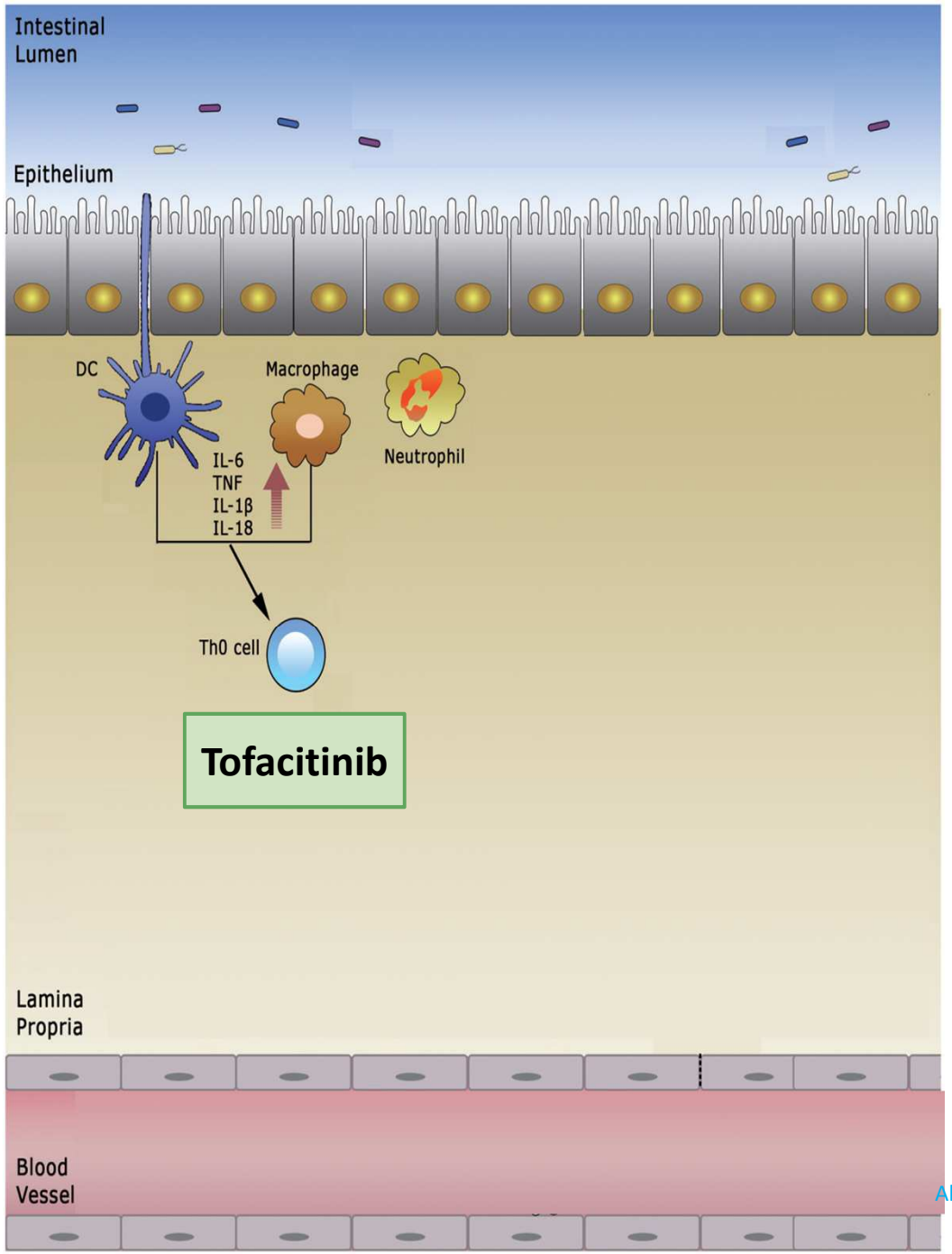
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



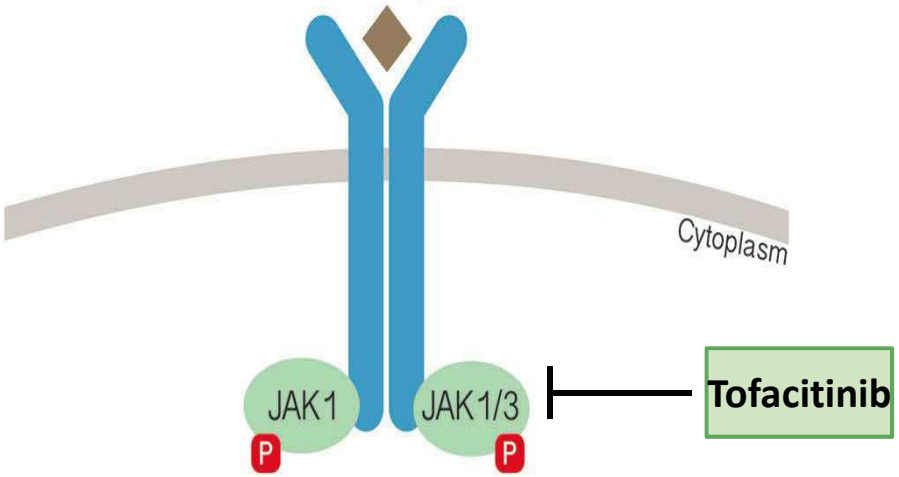
Ahluwalia A *et al. Scand J Gacstroenterol.* 2018;53:379-389.



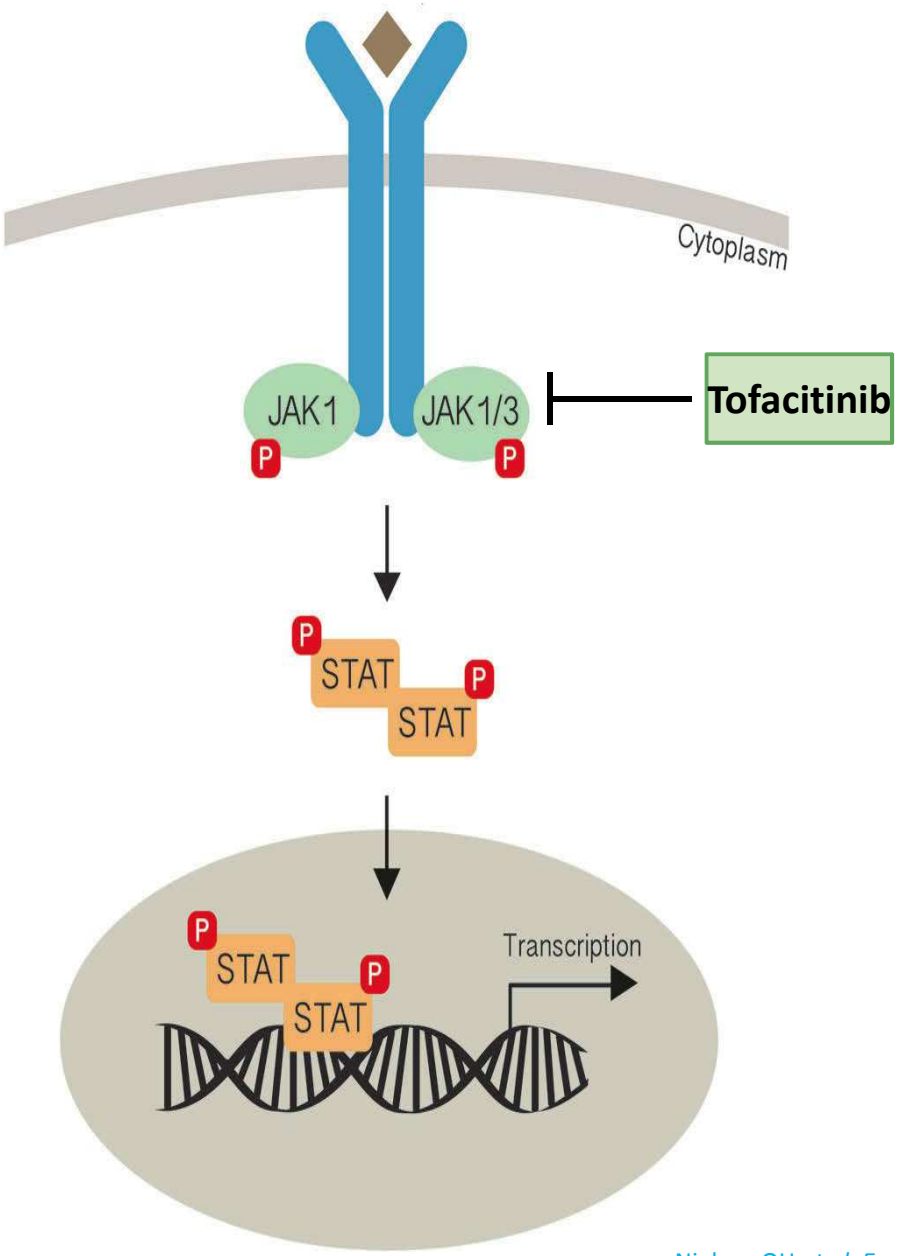
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



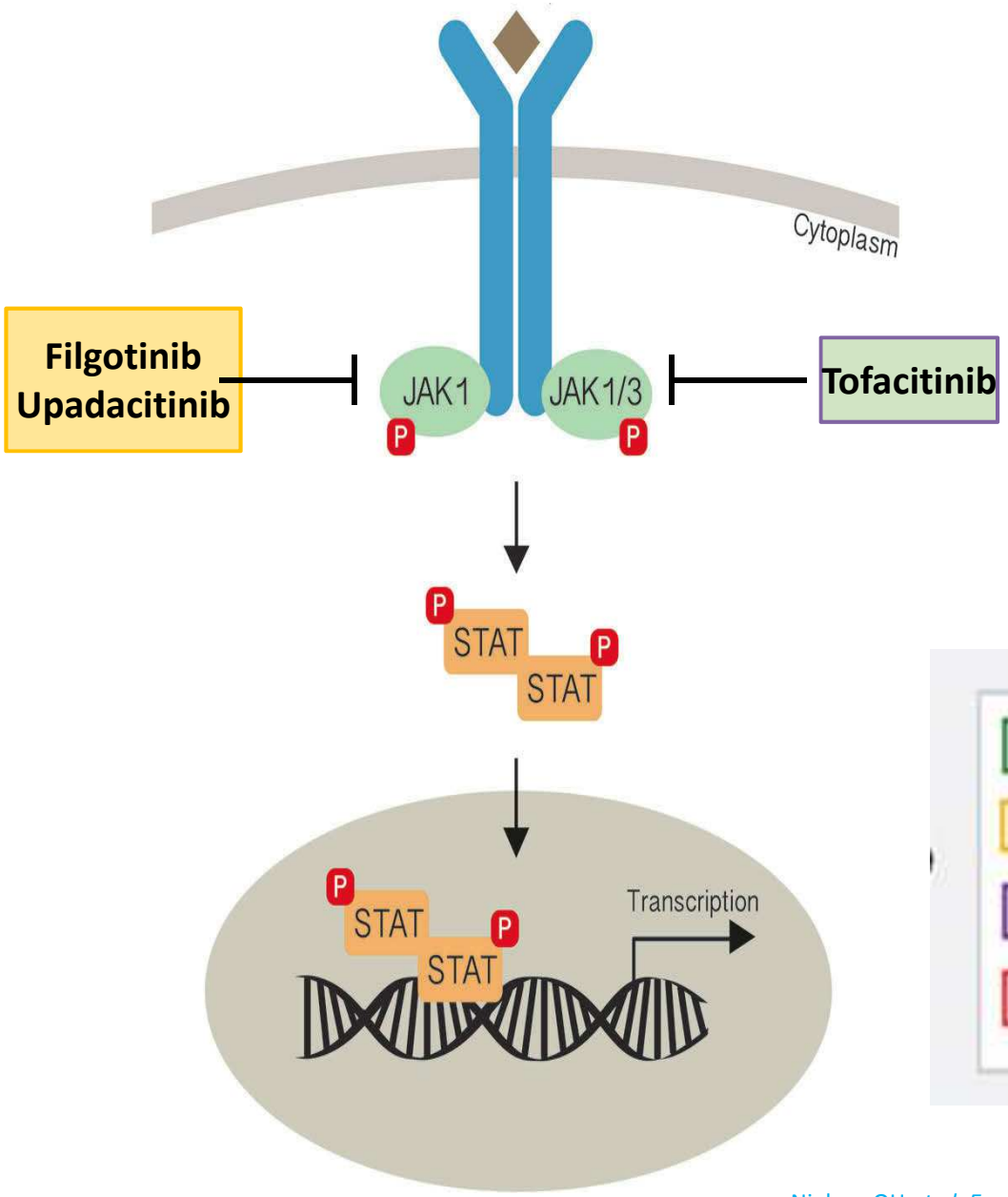
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



Nielsen OH *et al. Expert Opin Investig Drugs*. 2016;25:709-18



Nielsen OH *et al. Expert Opin Investig Drugs.* 2016;25:709-18



Nielsen OH *et al. Expert Opin Investig Drugs.* 2016;25:709-18

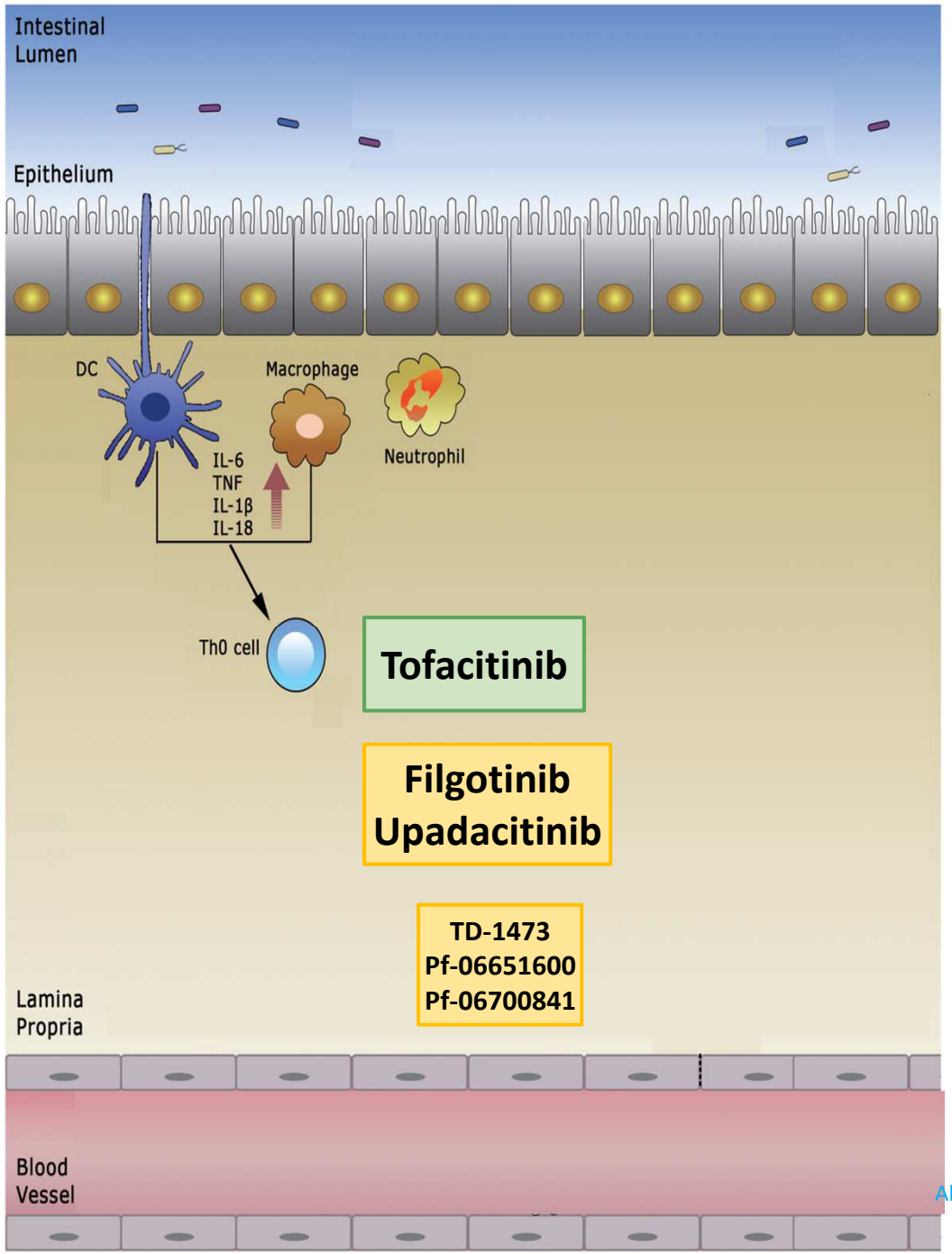
Cytokines	JAKs
IL-2	1 3
IL-7	1 3
IL-15	1 3
IL-21	1 3
IL-6*	1 2 T2
IL-13†	1 2 T2
IFN-γ	1 2
IL-22	1 T2
IL-12	2 T2
IL-23	2 T2
IL-5	2 2
IL-1β	-
IL-8	-
IL-17	-
IL-18	-
TNF-α	-

Danese S *et al. AJP Gastrointest Liver Physiol* 2016; 310: G155-G162

Cytokines	JAKs
	1 3
	1 3
	1 3
	1 3
IL-6	1 2 T2
	1 2 T2
	1 2
IL-22	1 T2
IL-12	2 T2
	2 T2
	2 2
	-
	-
	-
	-
	-

Danese S *et al. AJP Gastrointest Liver Physiol* 2016; 310: G155-G162

Cytokines	JAKs	
	1 3	
	1 3	
	1 3	
	1 3	
IL-6	1 2 T2	**Barrière épithéliale**
	1 2 T2	
	1 2	
IL-22	1 T2	**Cicatrisation, barrières**
IL-12	2 T2	
	2 T2	
	2 2	
	-	
	-	
	-	
	-	
	-	



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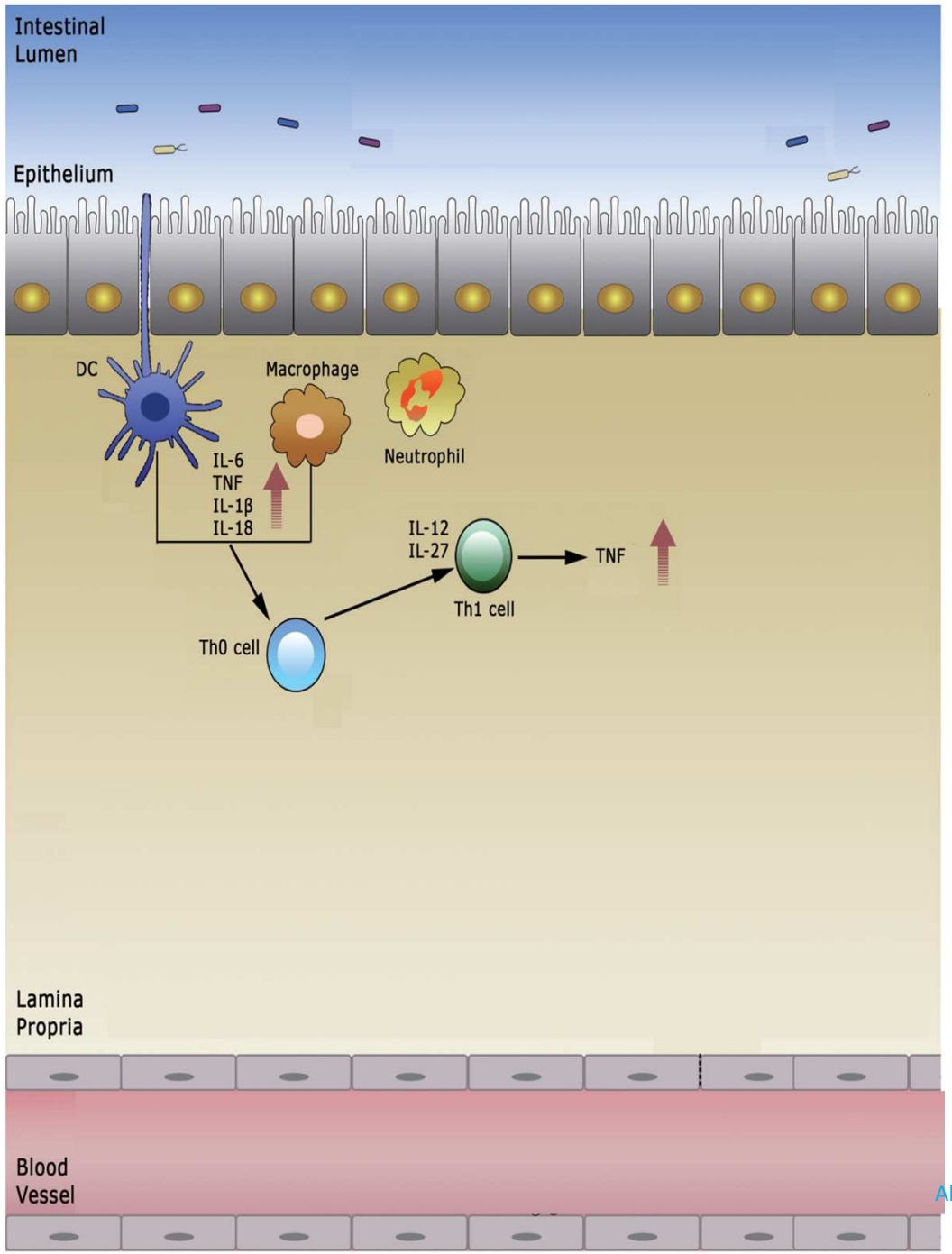
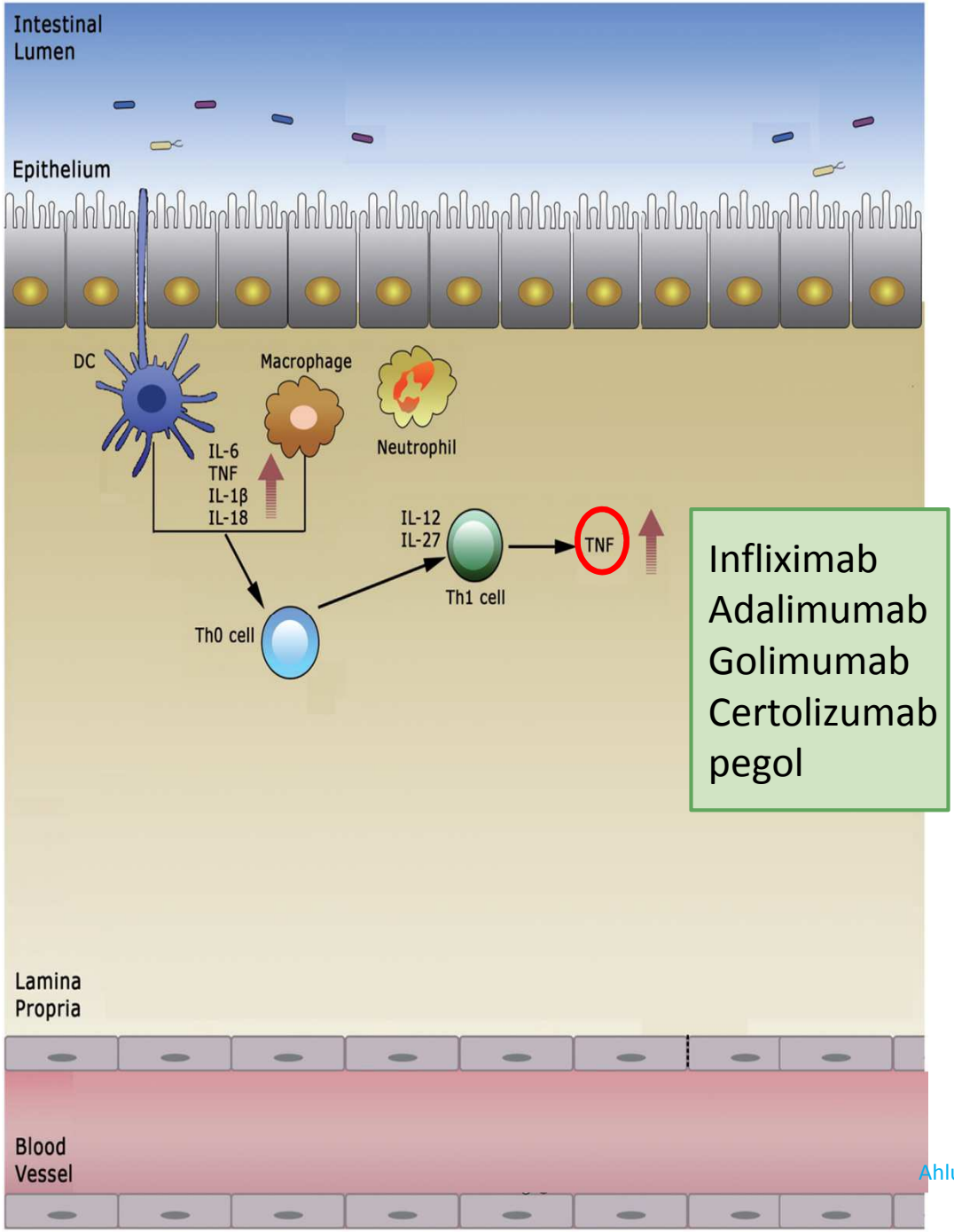
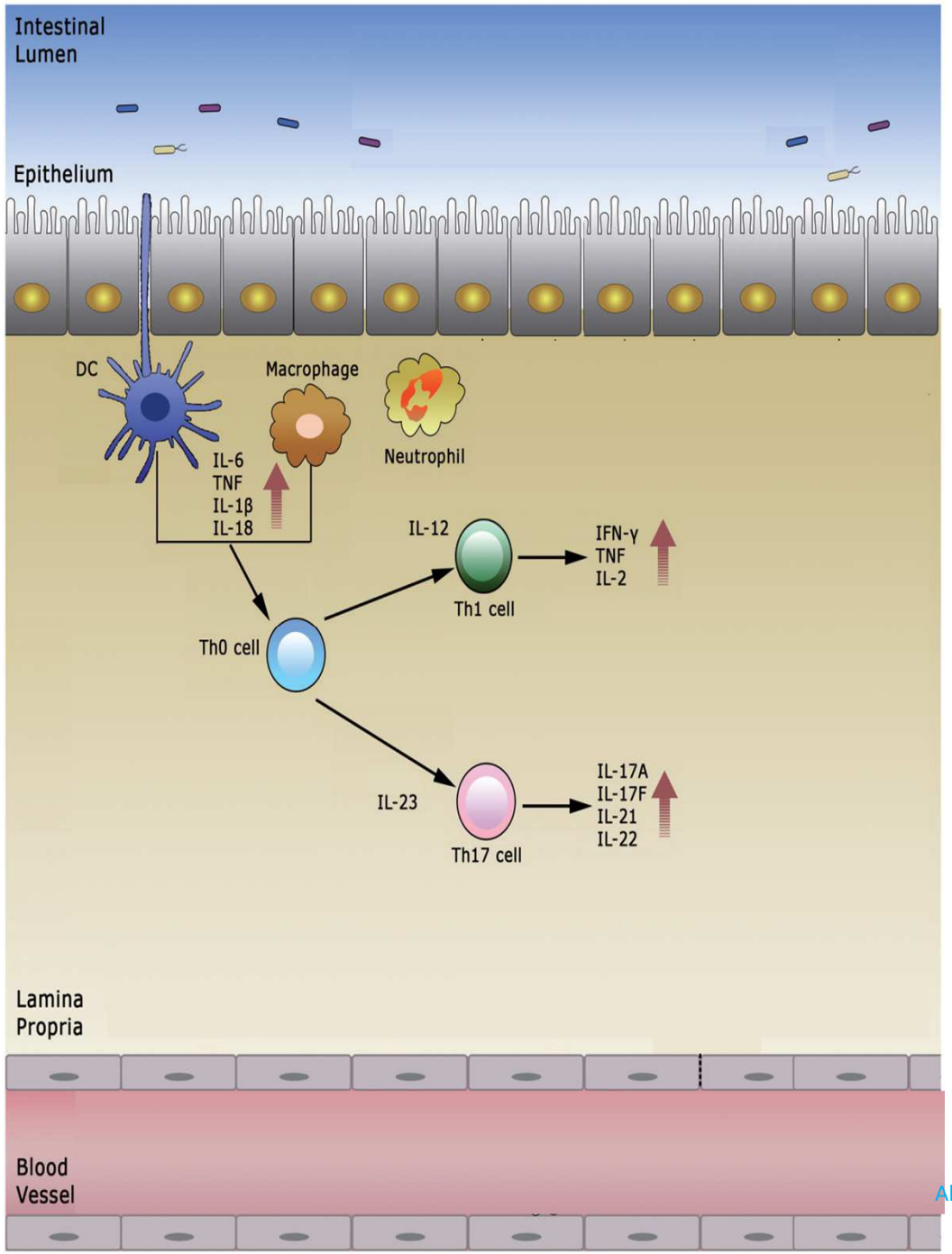


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



Infliximab
Adalimumab
Golimumab
Certolizumab pegol

Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



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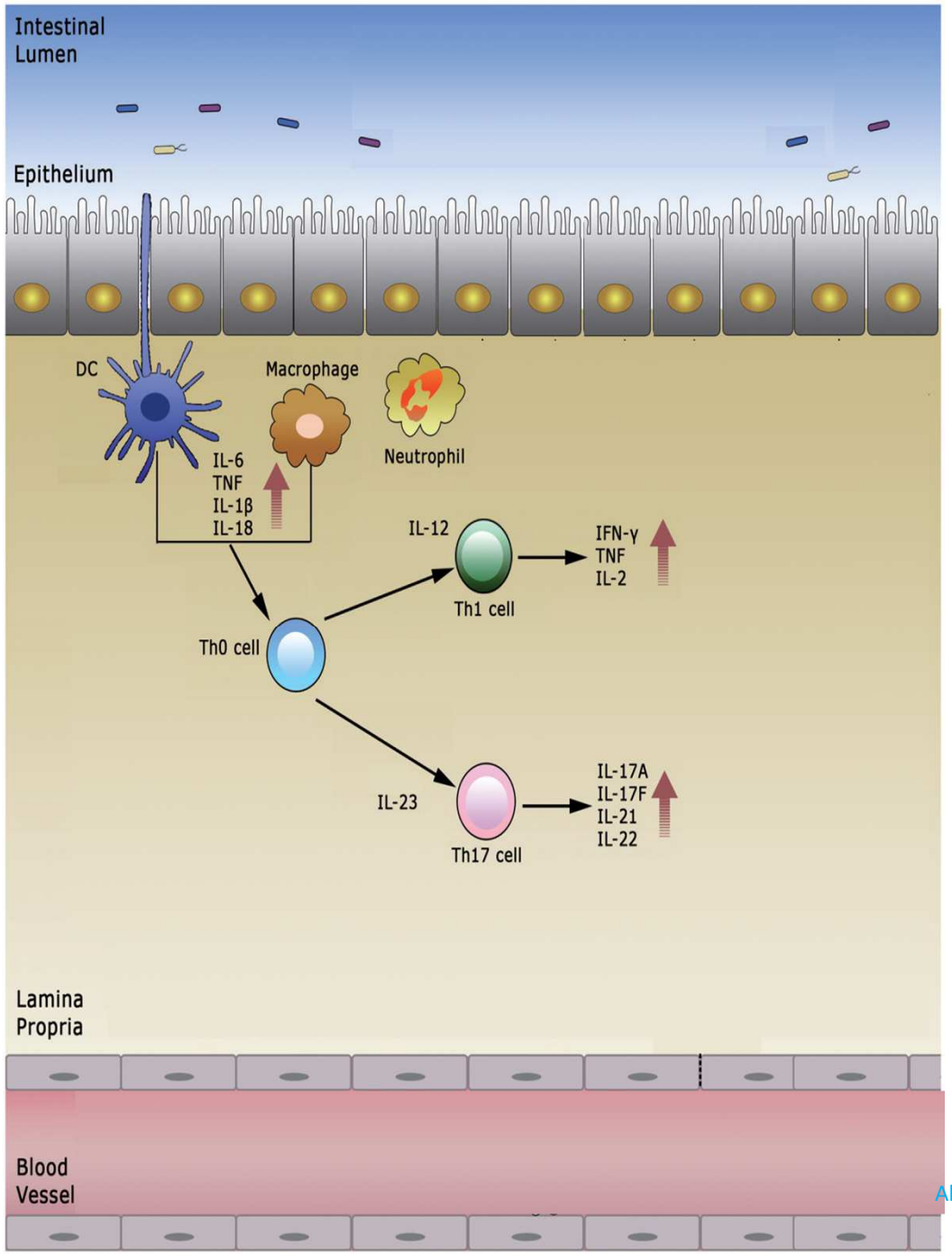

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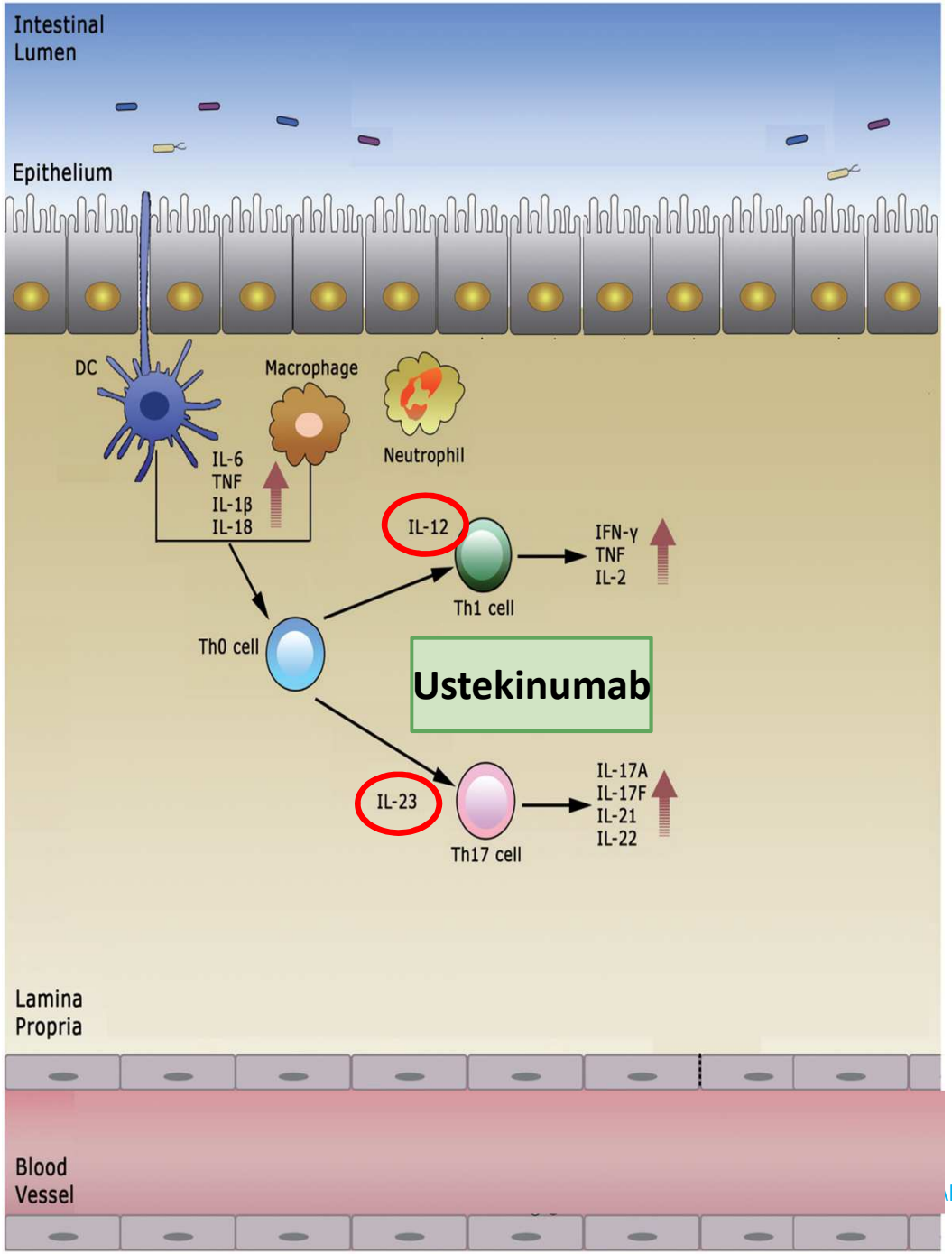

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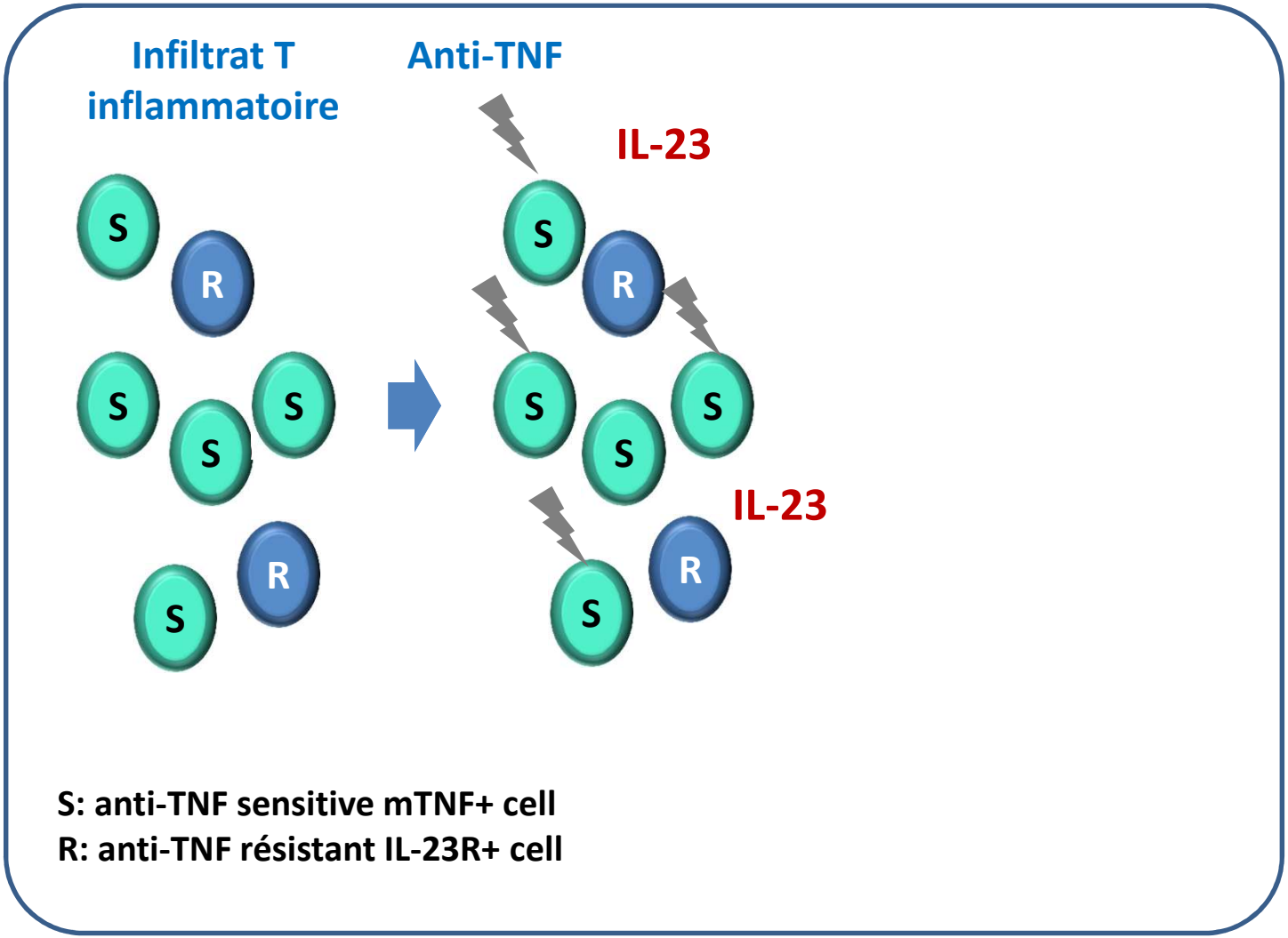
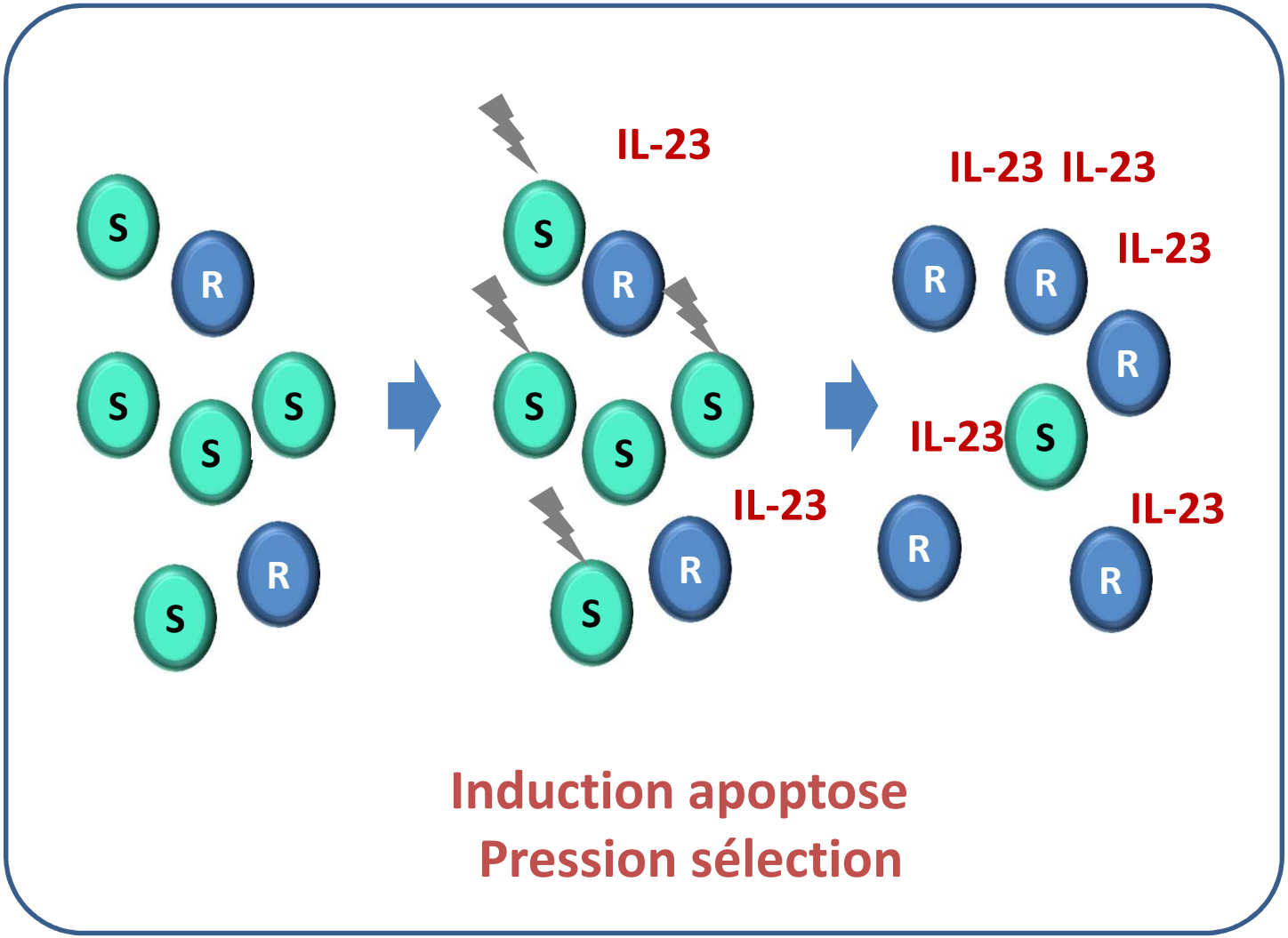
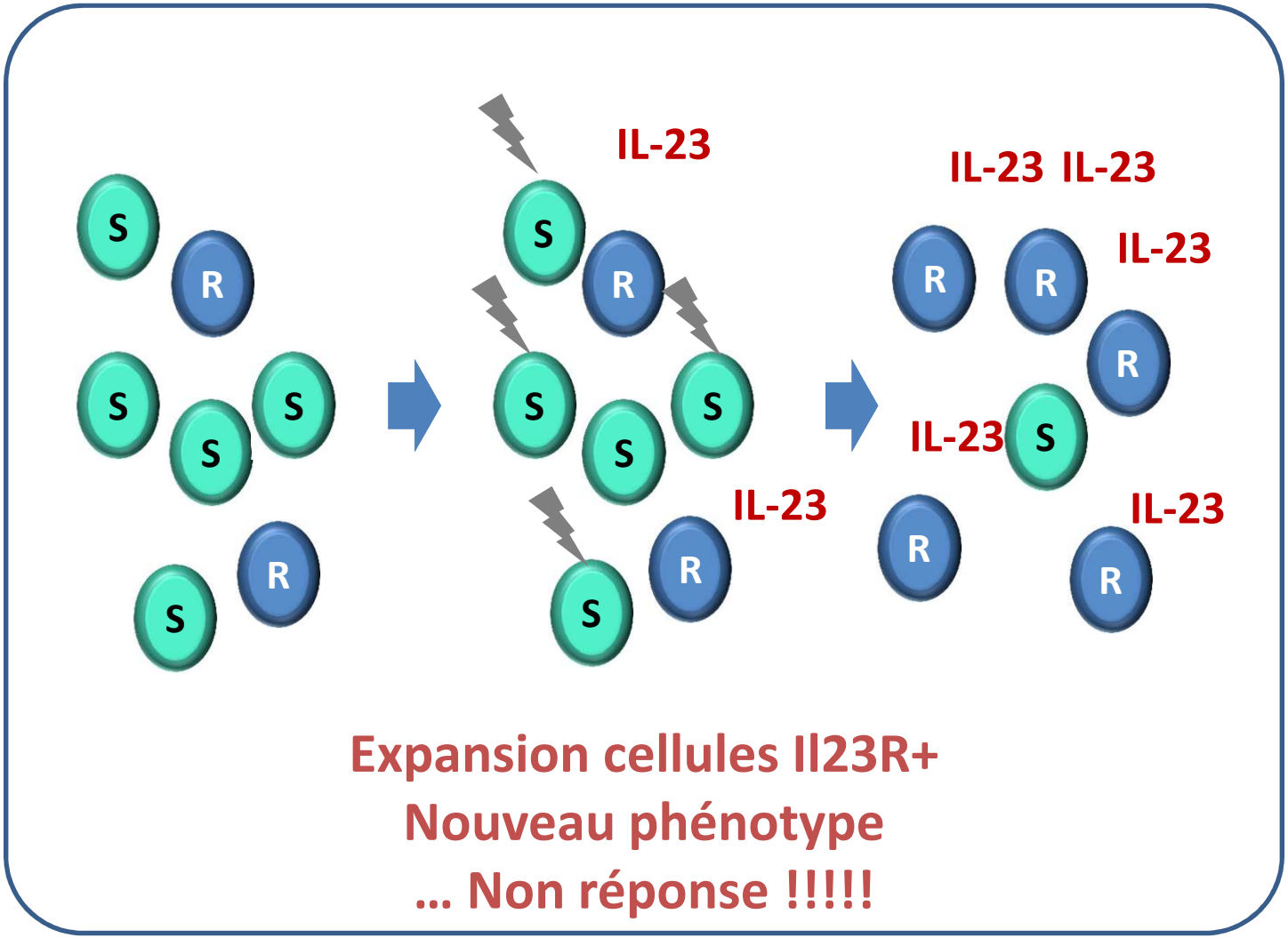


Schmitt H, *et al. Gut* 2018;0:1-15. doi:10.1136/gutjnl-2017-315671

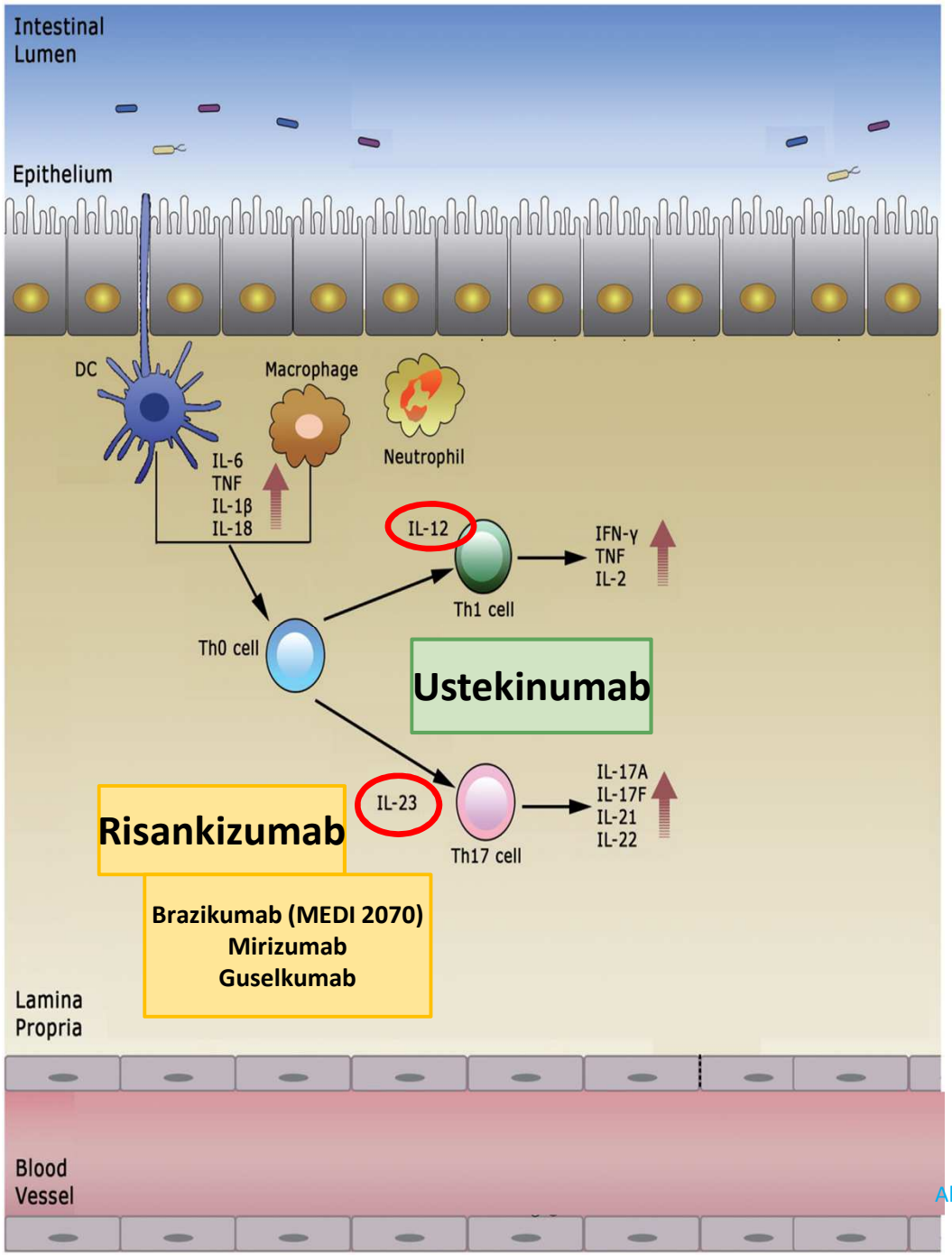


Schmitt H, *et al. Gut* 2018;0:1-15. doi:10.1136/gutjnl-2017-315671

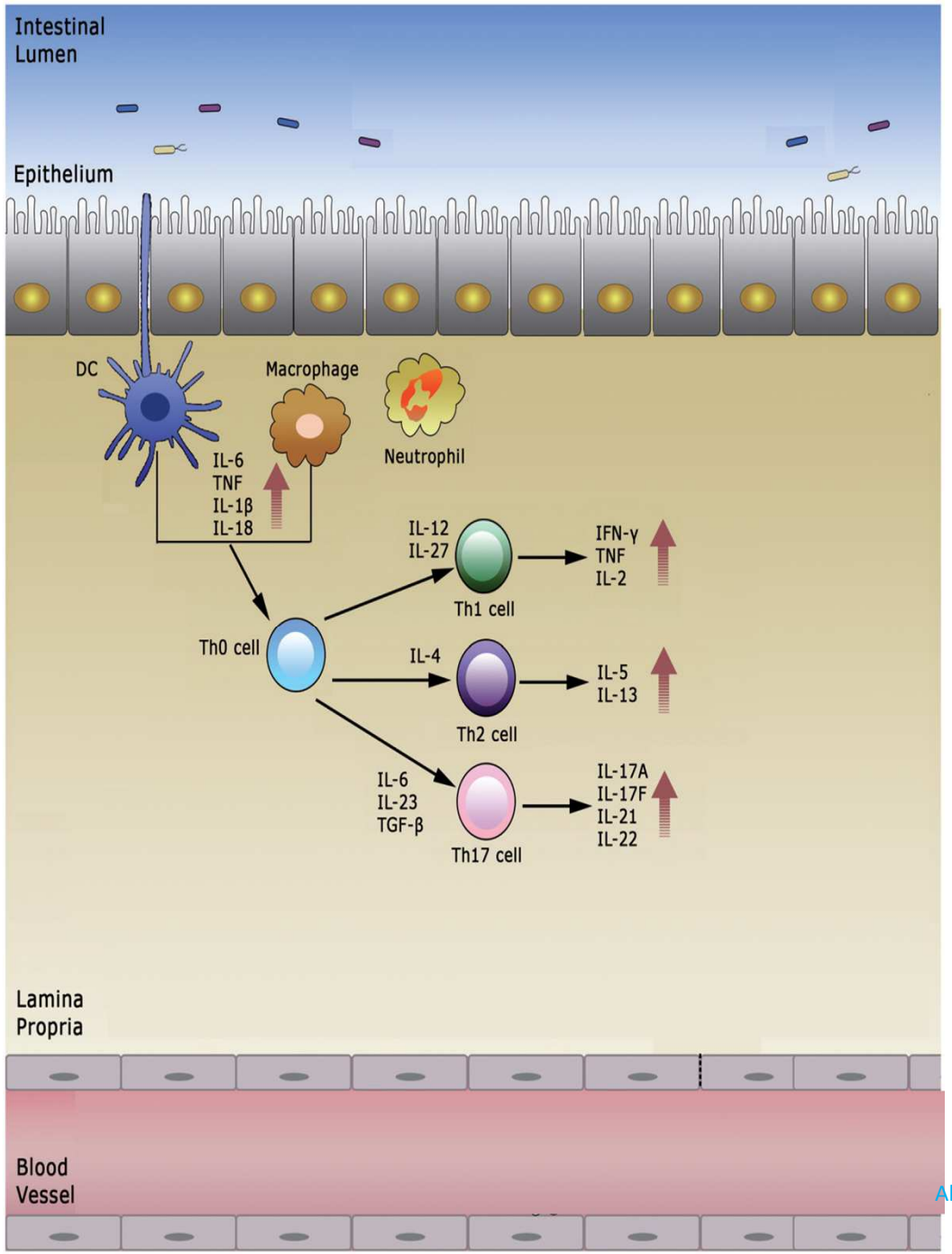
Résistance moléculaire Il23 à l'a-TNF



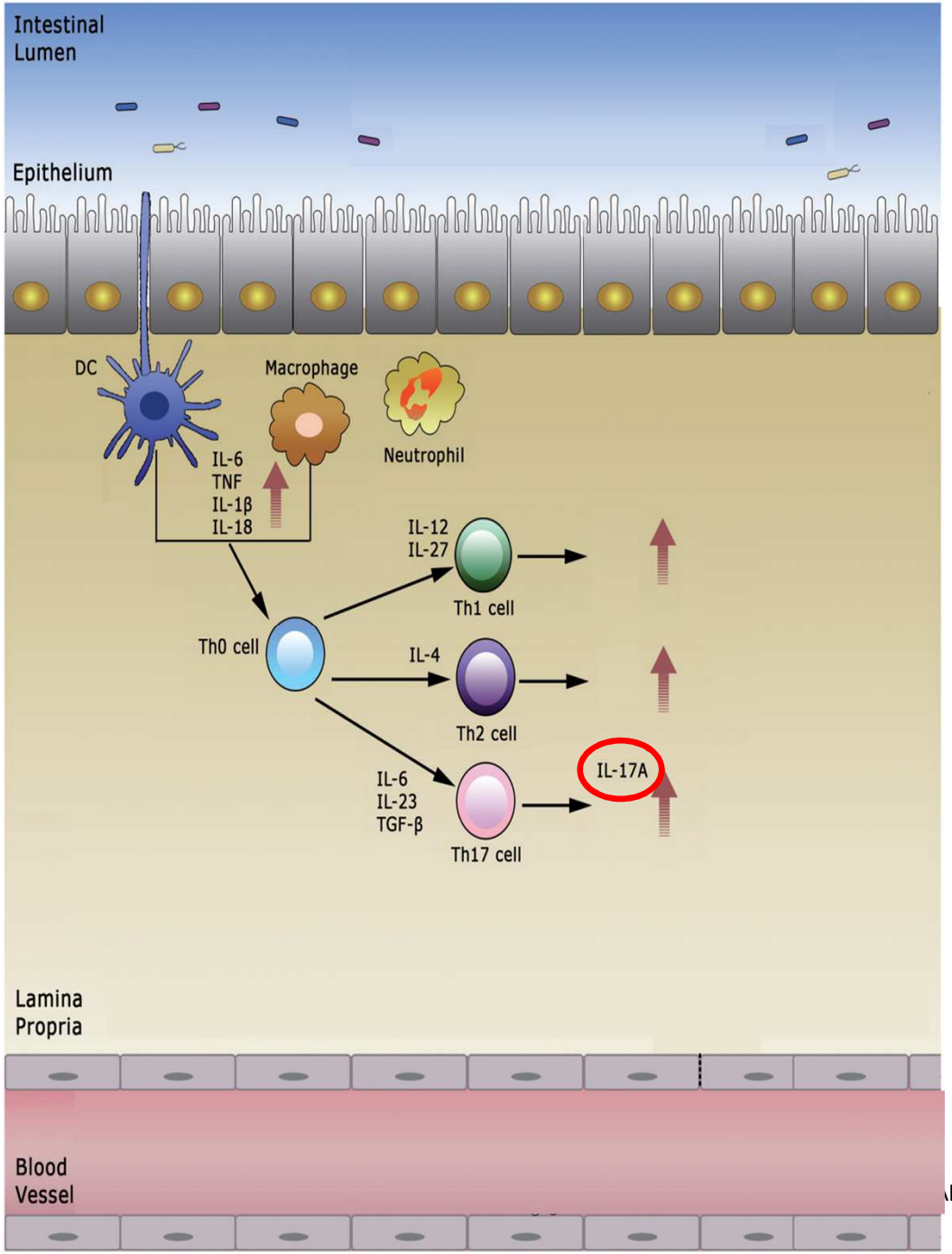
Schmitt H, *et al. Gut* 2018;0:1-15. doi:10.1136/gutjnl-2017-315671



Ahluwalia A *et al. Scand J Gastroenterol*. 2018;53:379-389.

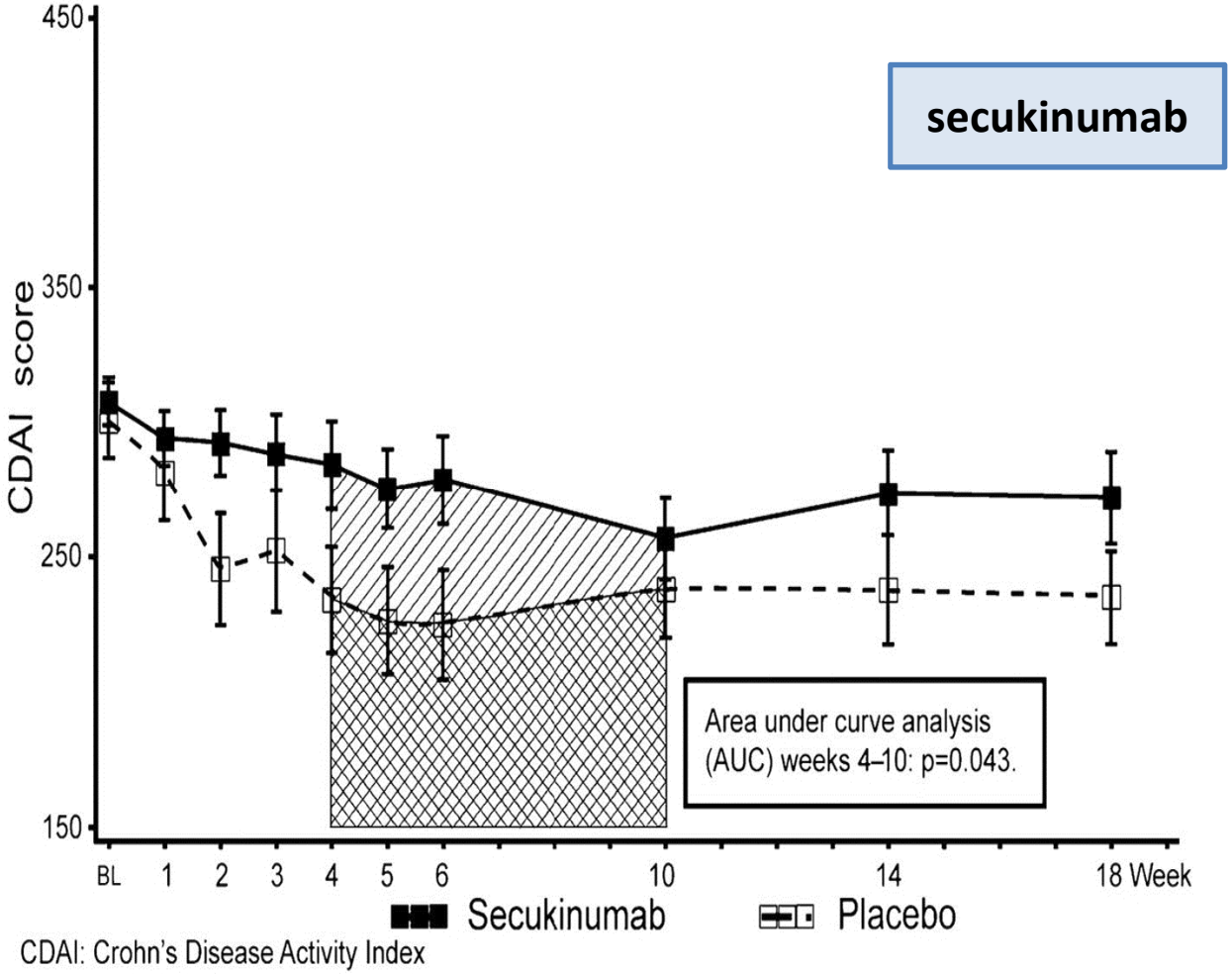


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

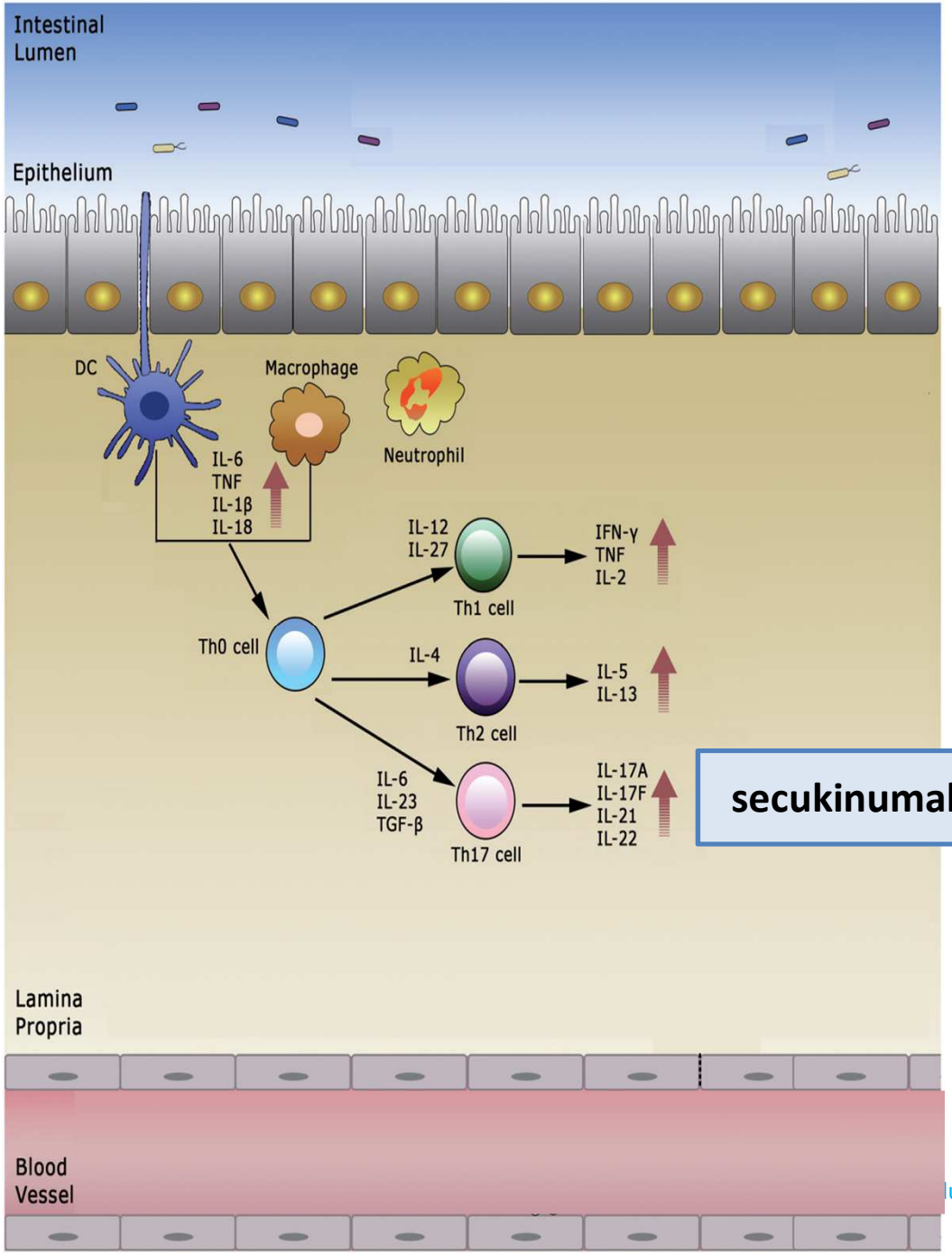


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

Blocage Il17A dans Crohn



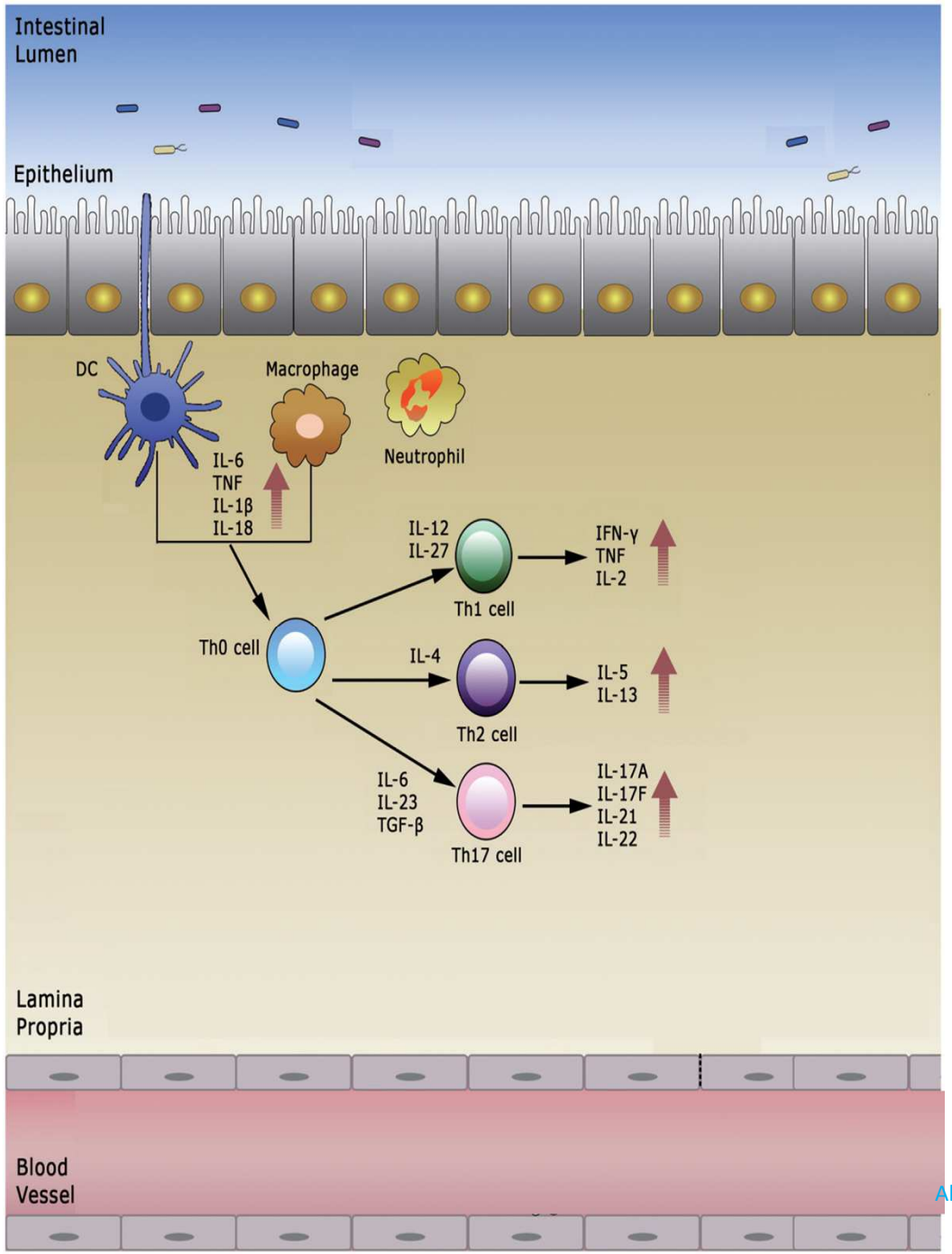
Hueber W *et al. Gut.* 2012;61:1693-700



secukinumab

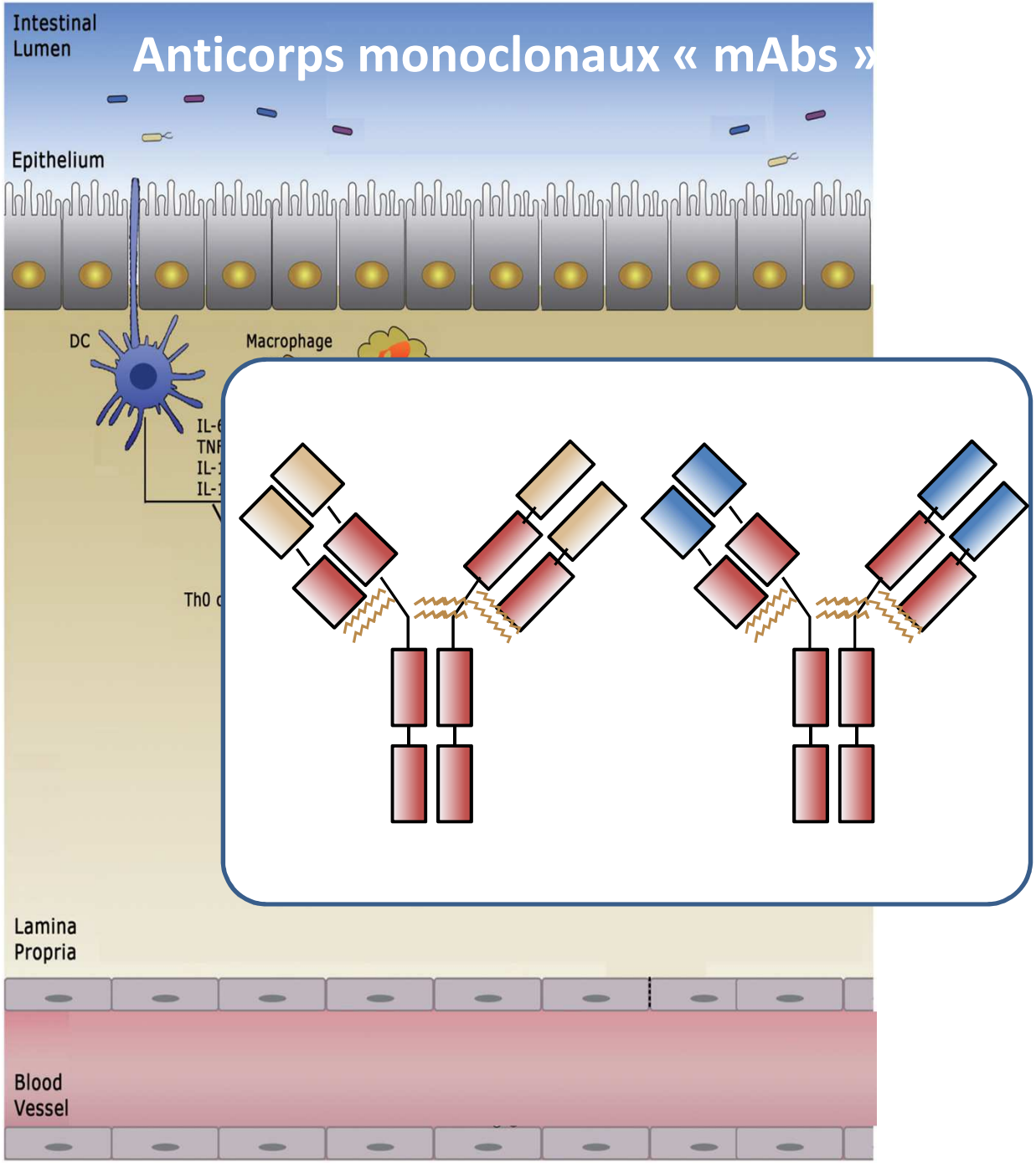
Schreider S *et al. Ann Rheum dis.* 2019 Jan 23.

luwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

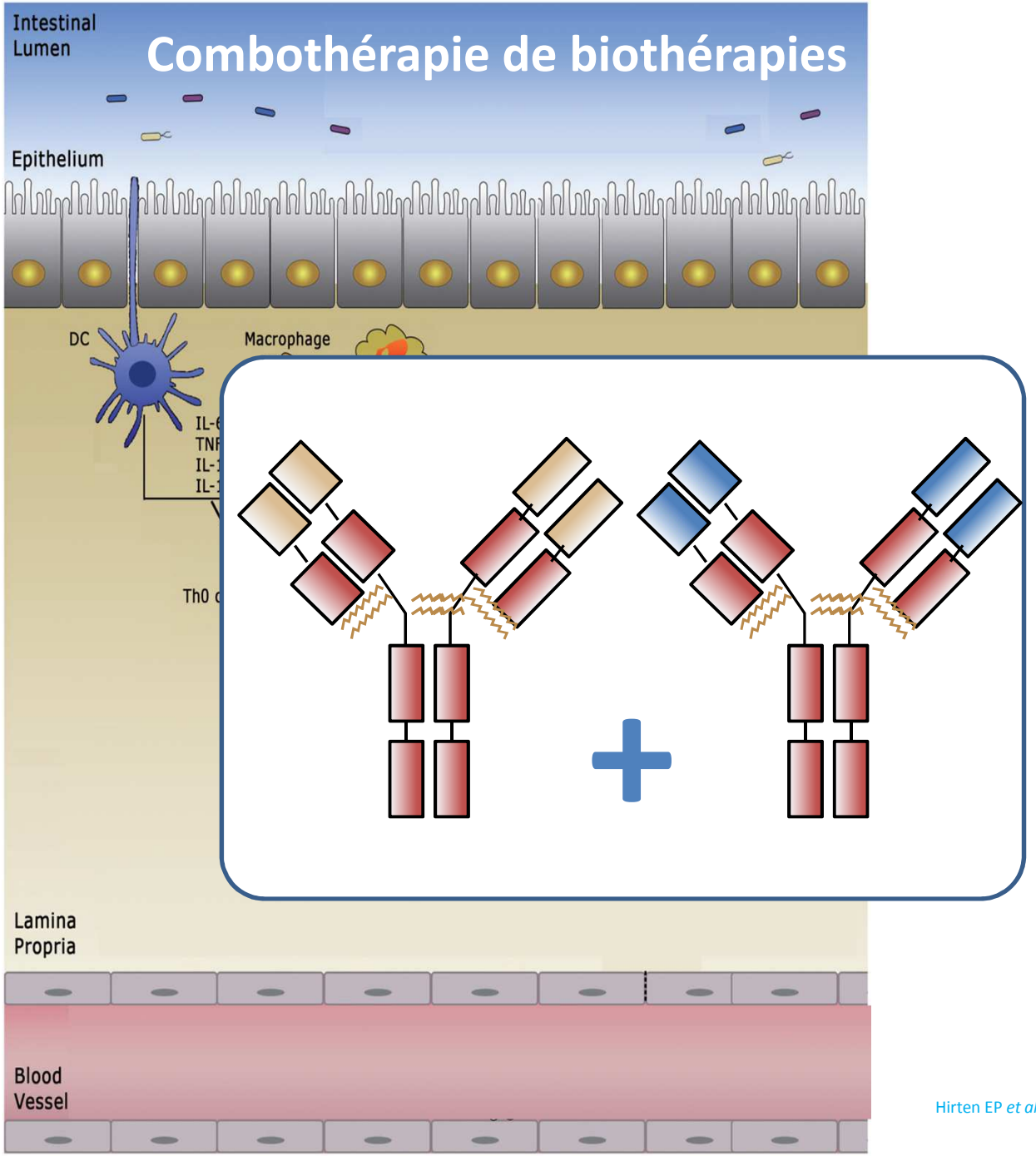


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

Anticorps monoclonaux « mAbs »

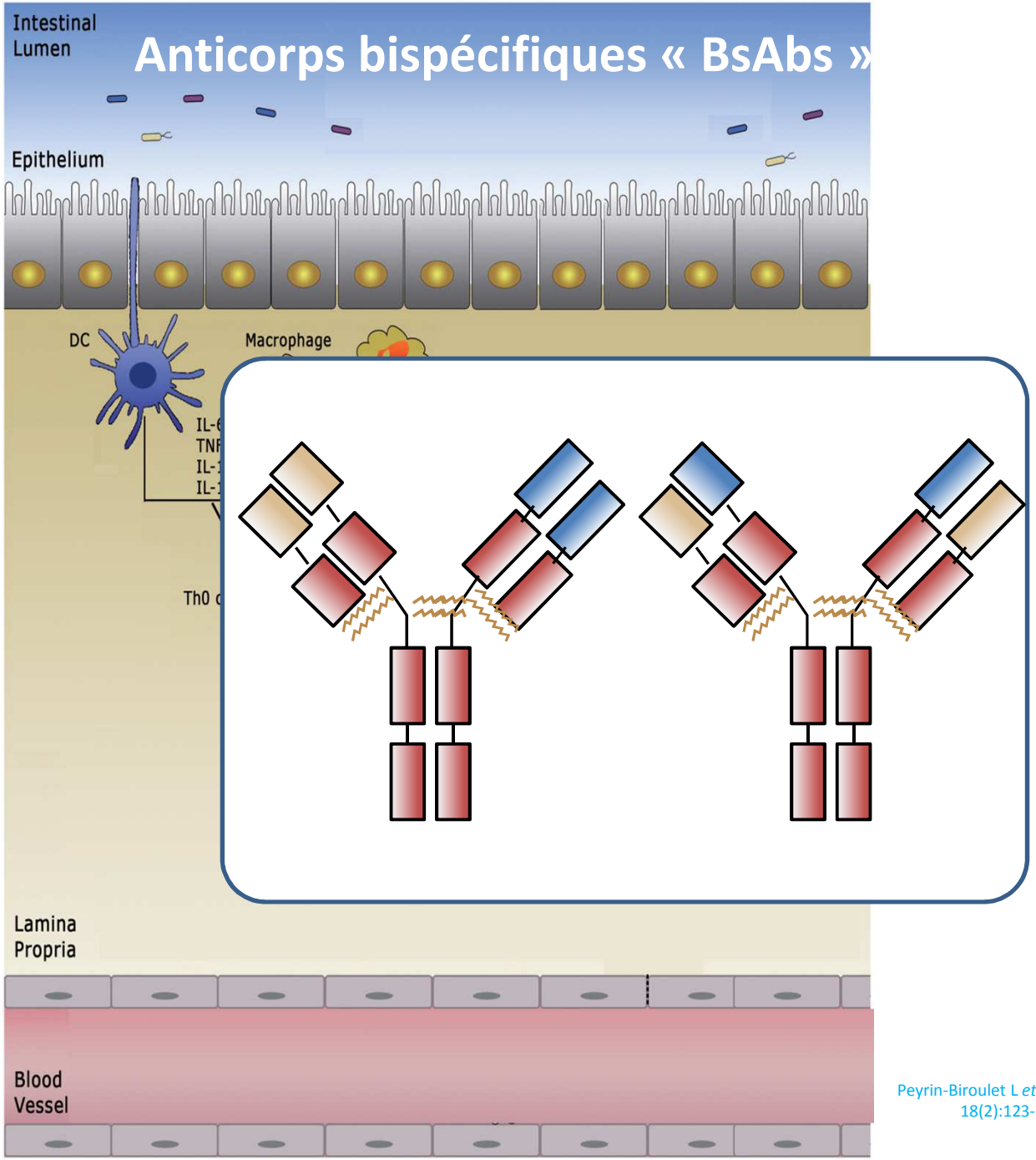


Combothérapie de biothérapies

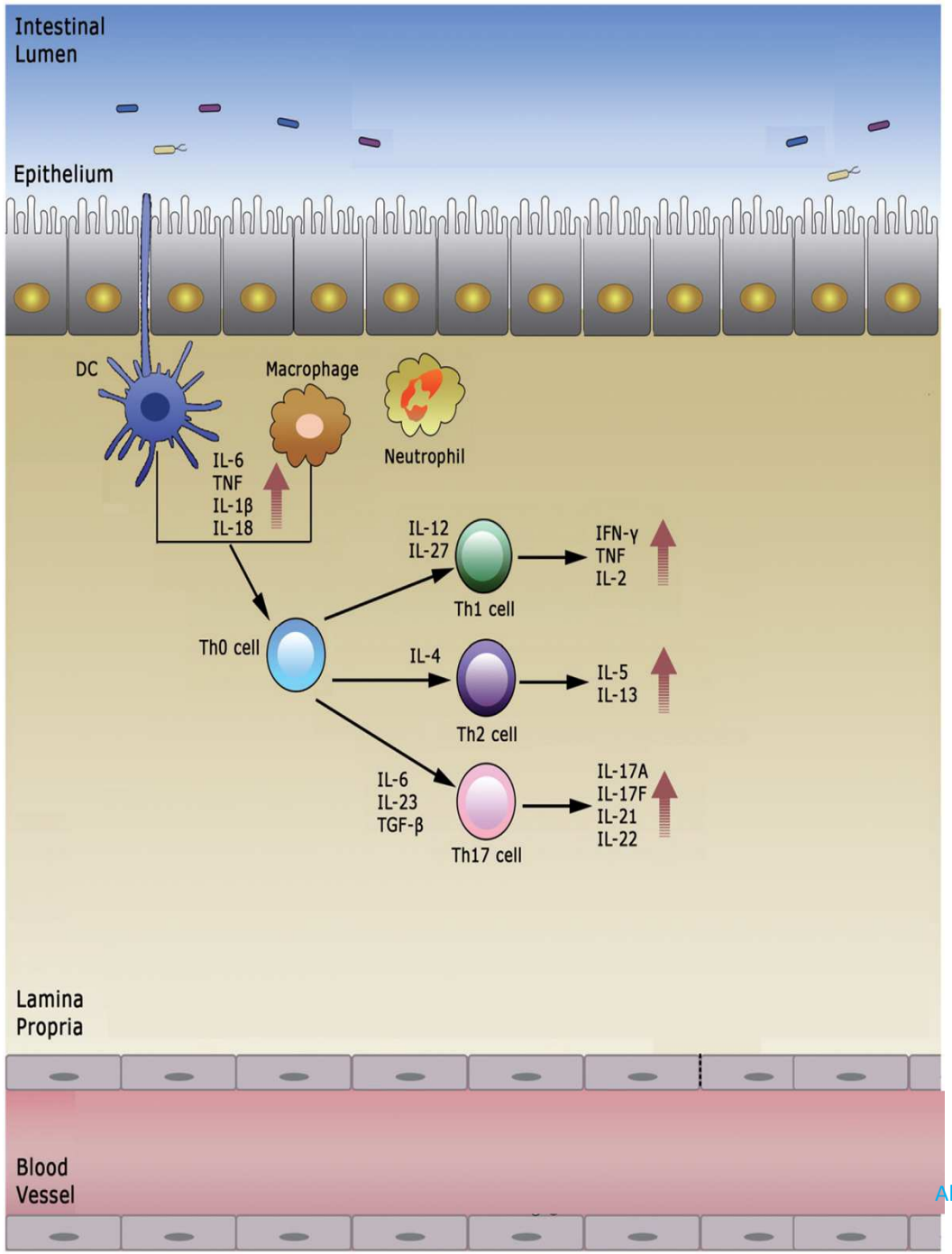


Hirten EP *et al.Clinical Gastroenterology* 2018;16:1374-1384

Anticorps bispécifiques « BsAbs »



Peyrin-Biroulet L *et al. Autoimmun Rev*. 2019; 18(2):123-128. doi: 10:1016/j.autrev. 2018.07.014.



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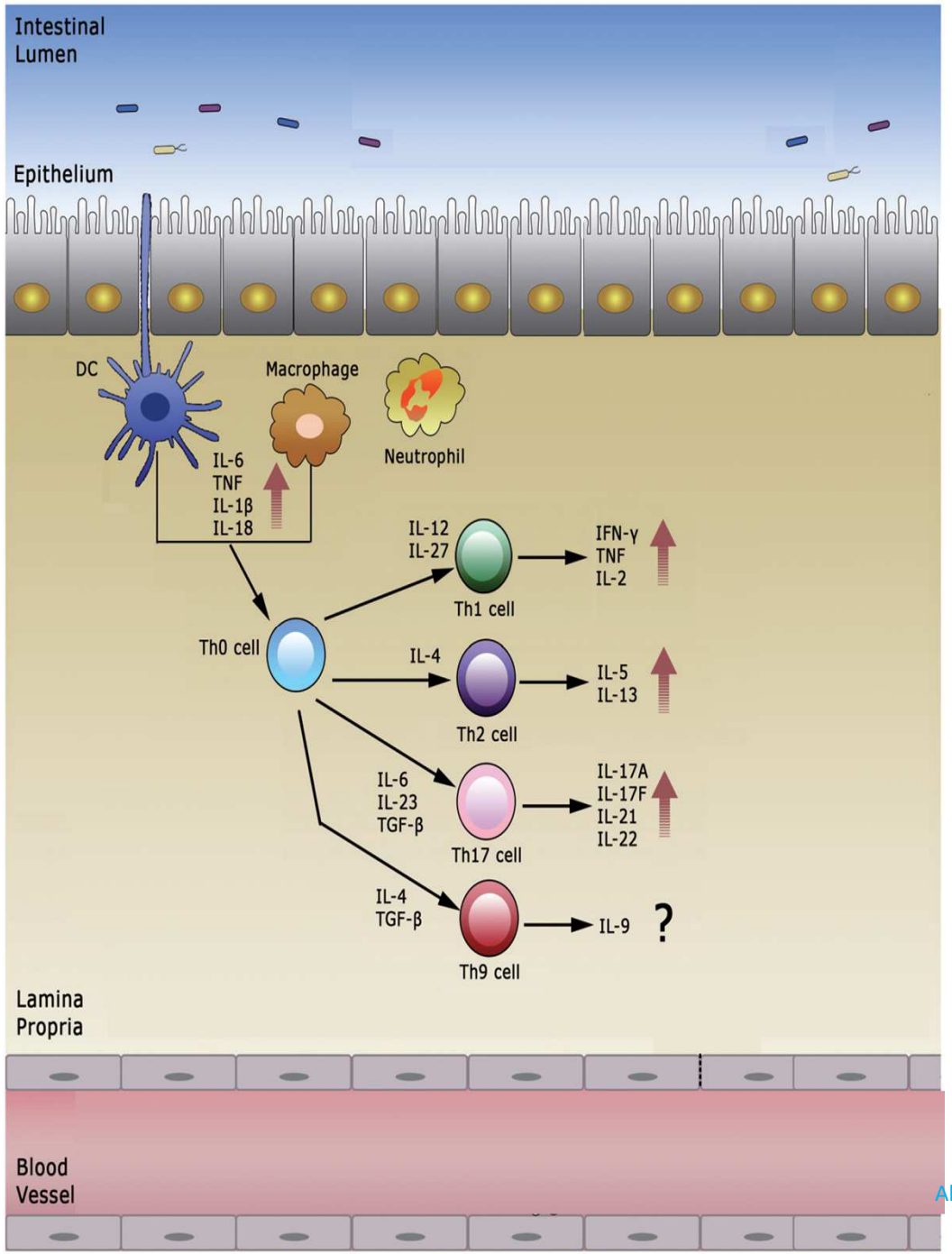

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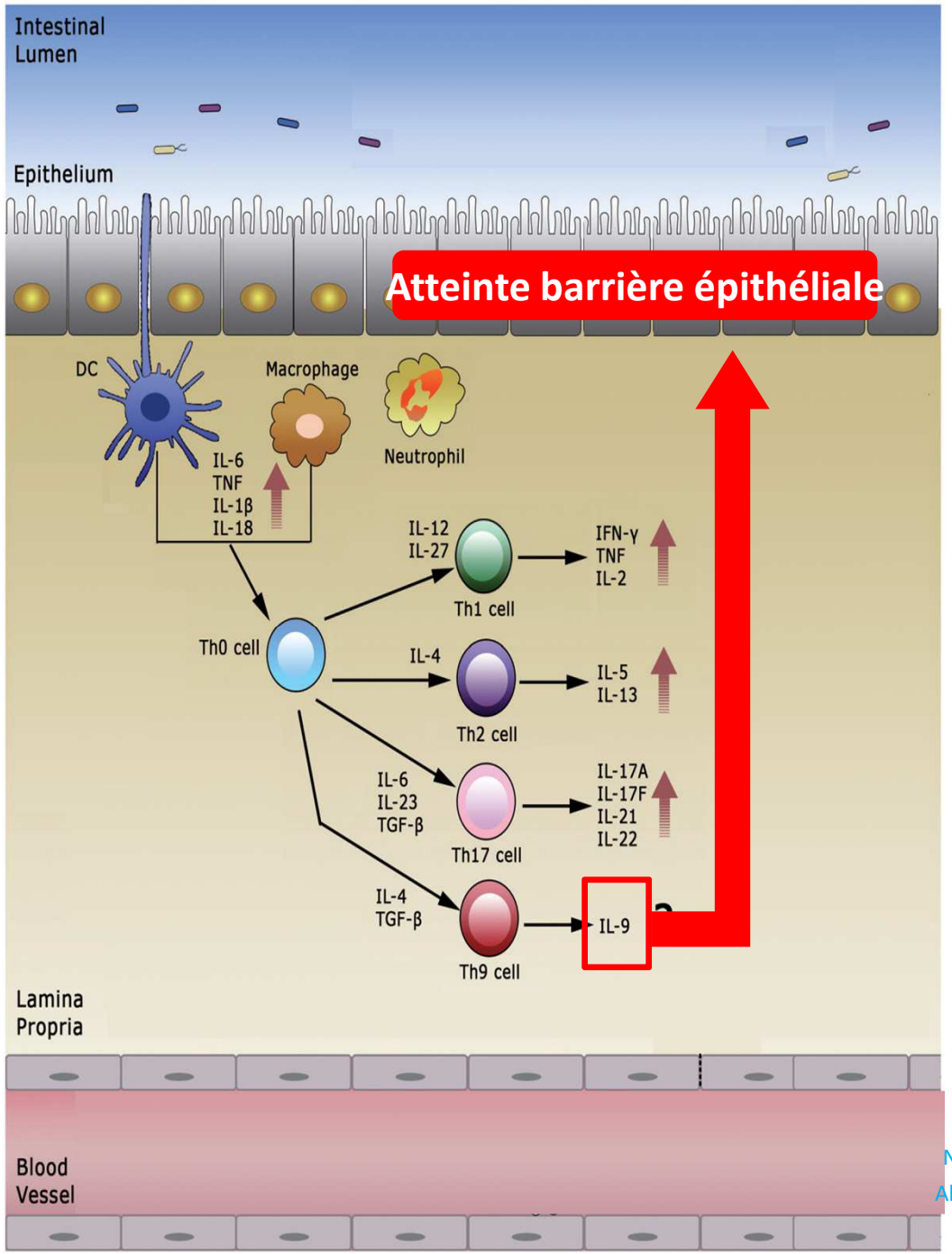
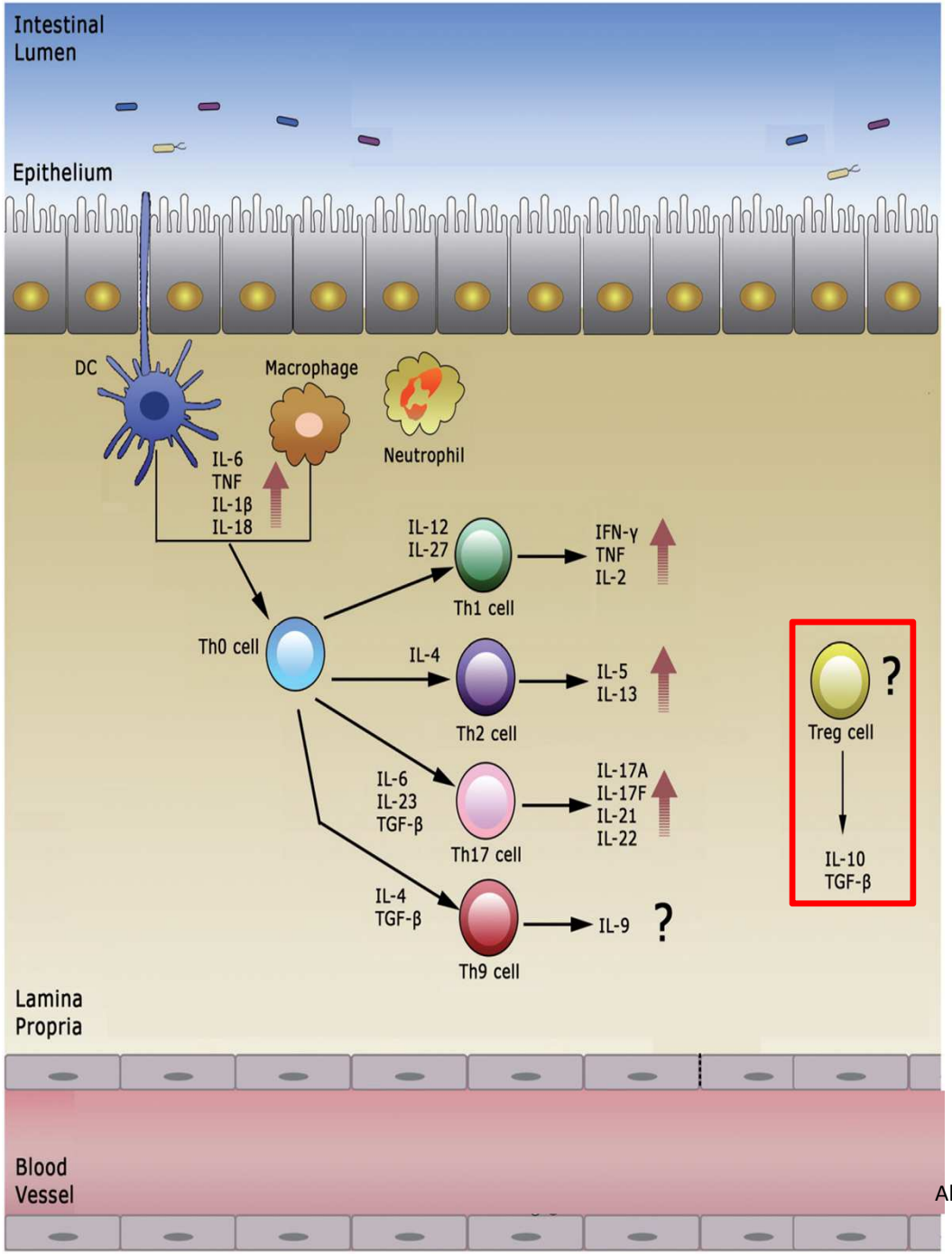


Nalleweg N *et al. Gut* 2015; 64:743-755

Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



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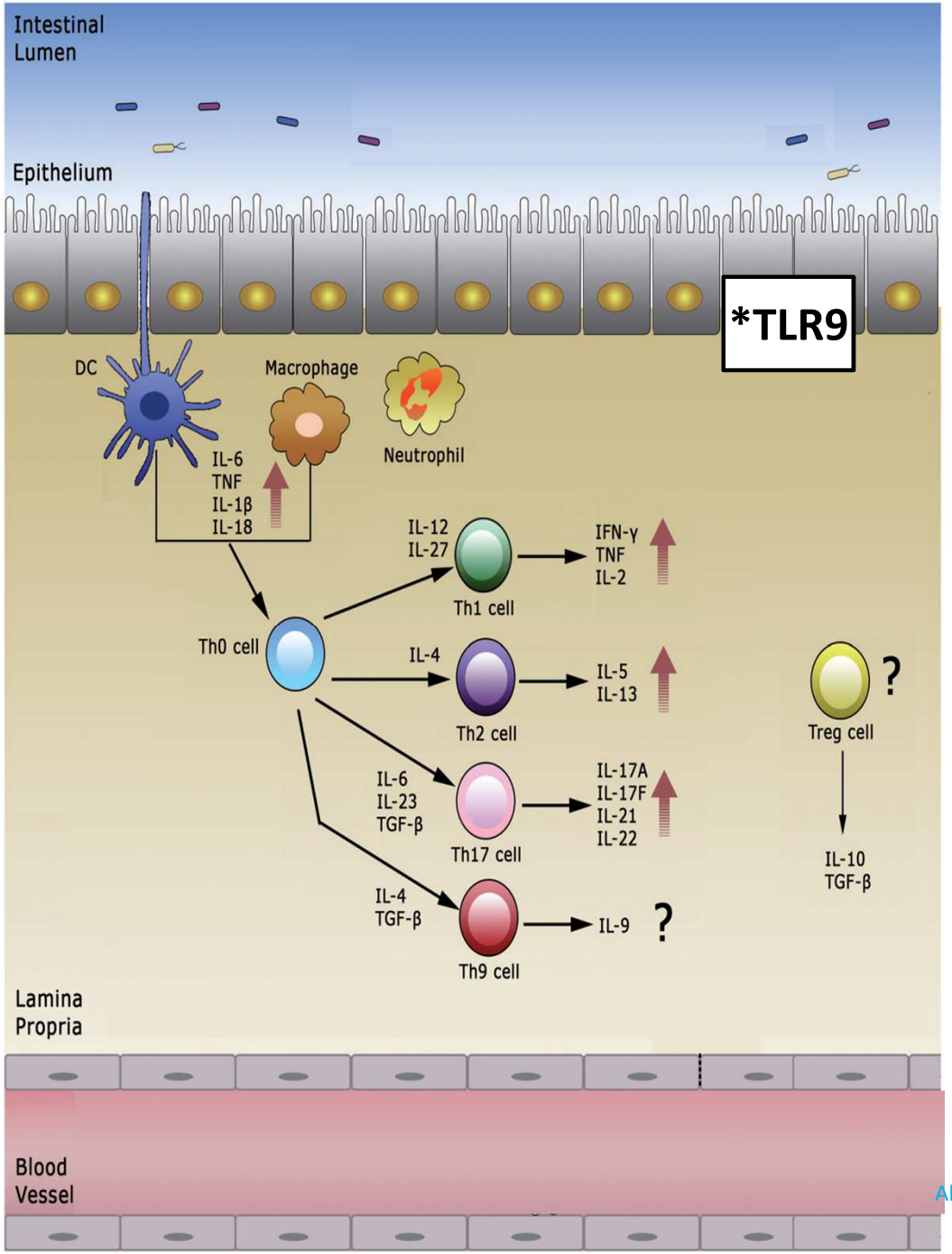

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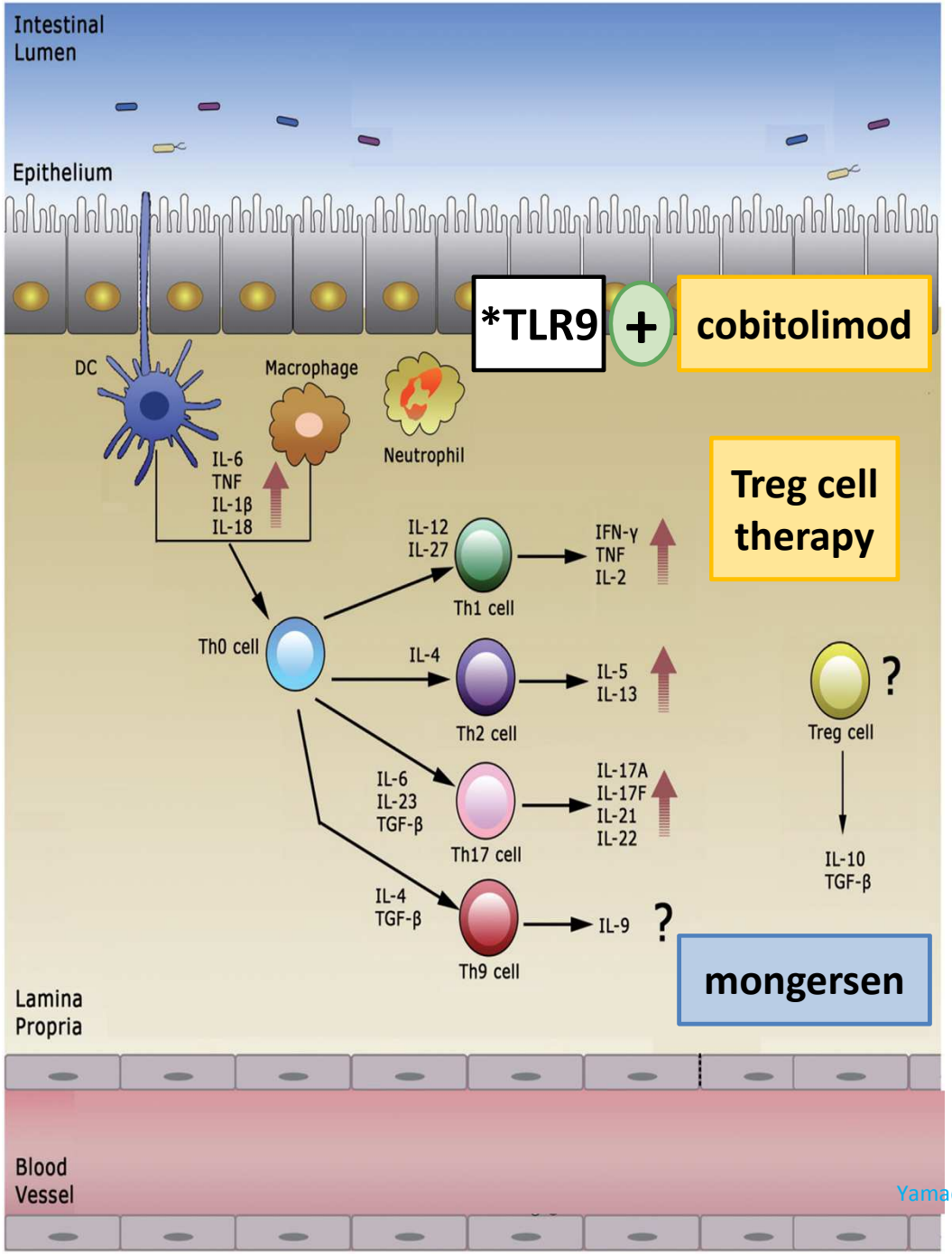
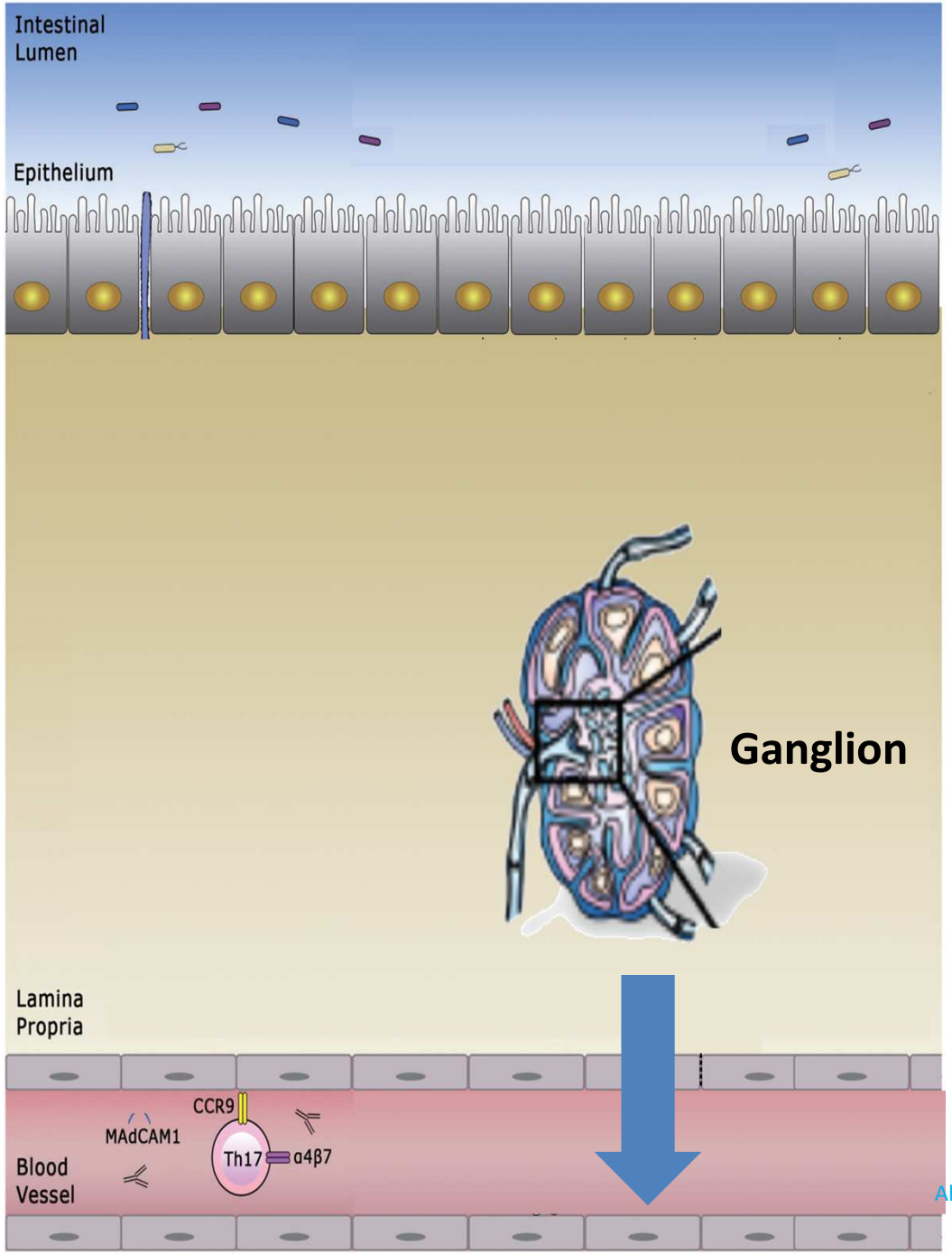
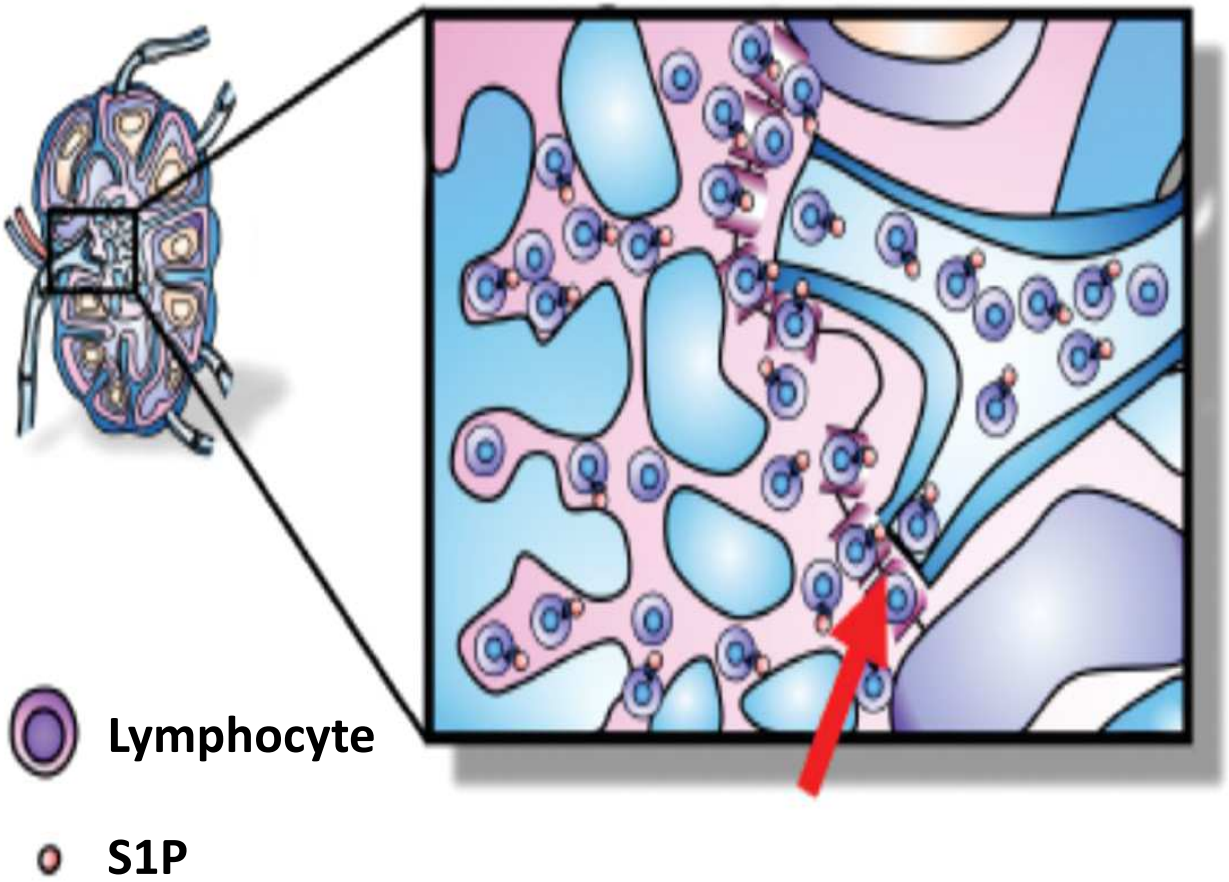


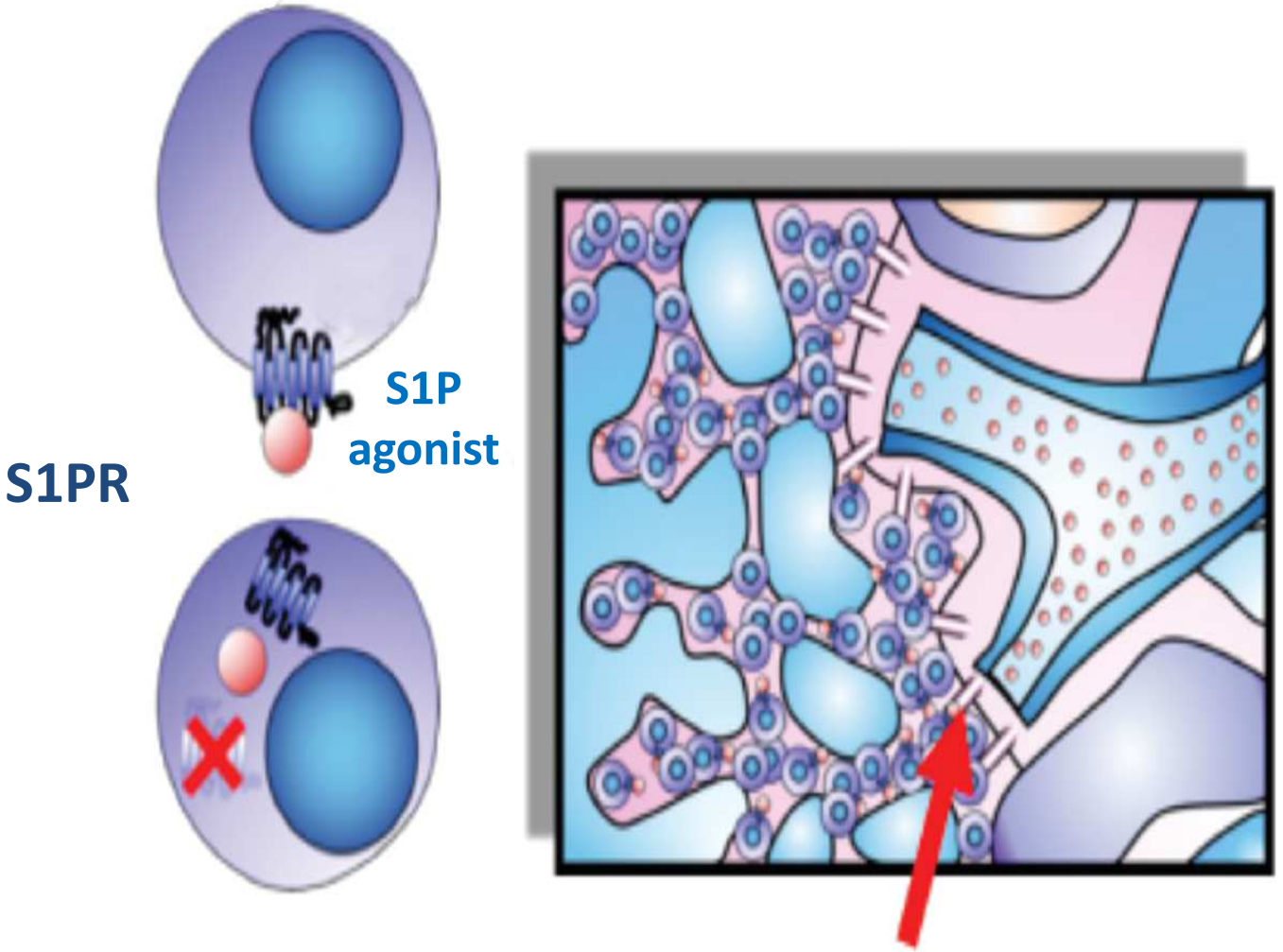
Yamada A *et al. World J Gastroenterol* 2016; 22: 2195-2205



Ahluwalia A et al. Scand J Gastroenterol. 2018;53:379-389



Pérez-Jeldres T *et al. IBD* 2018; doi:10.1093/ibd/izy269



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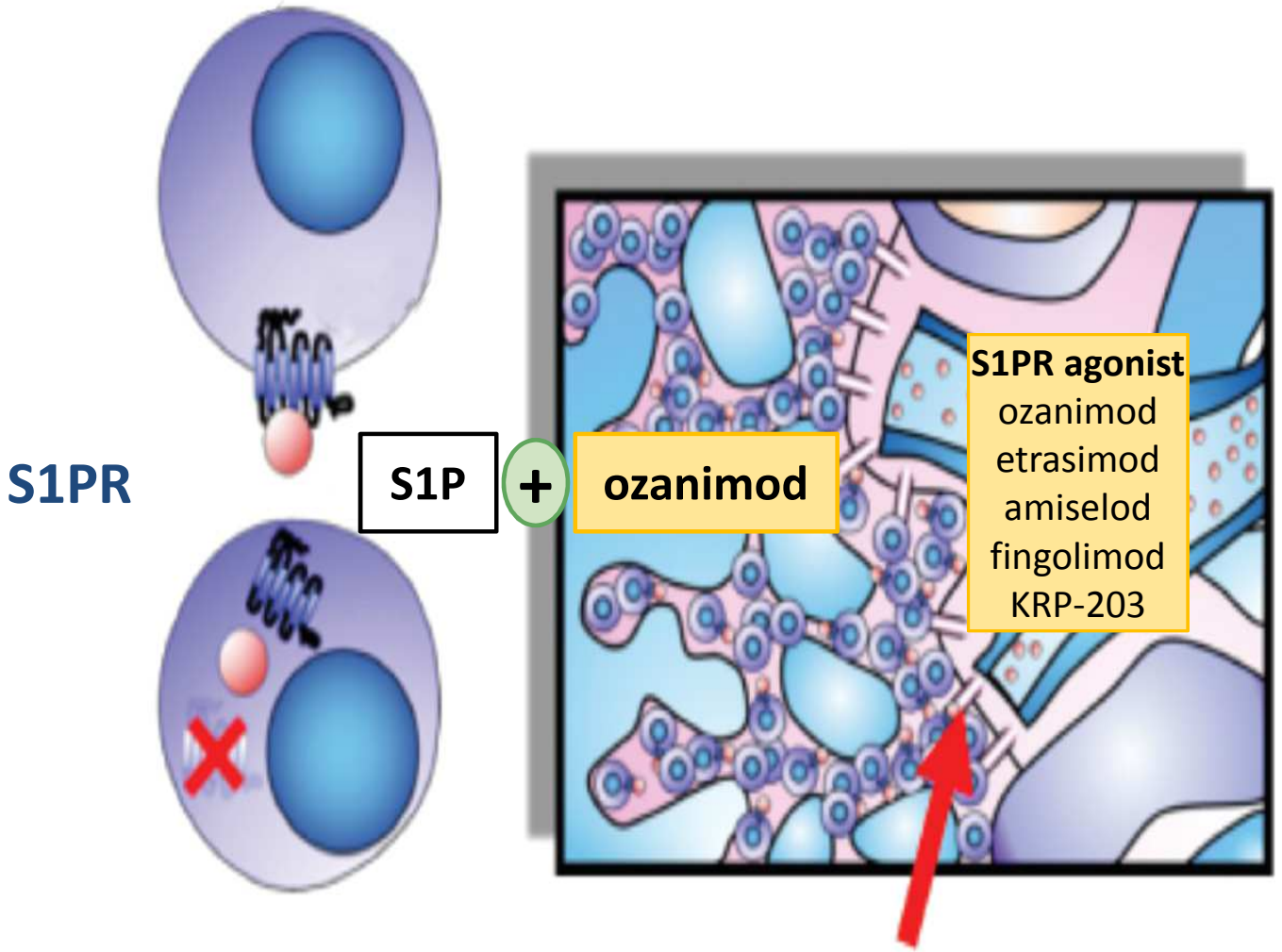

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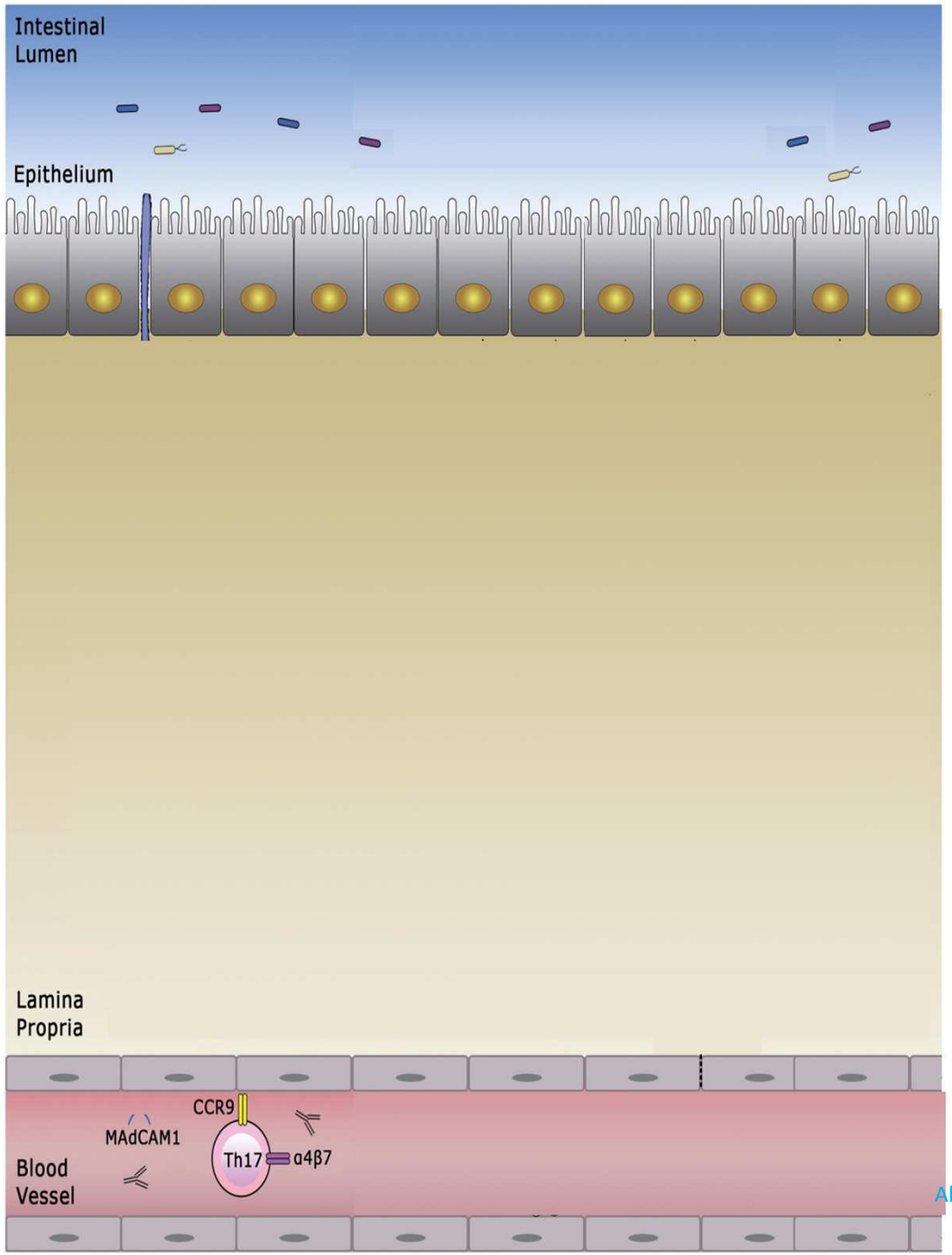
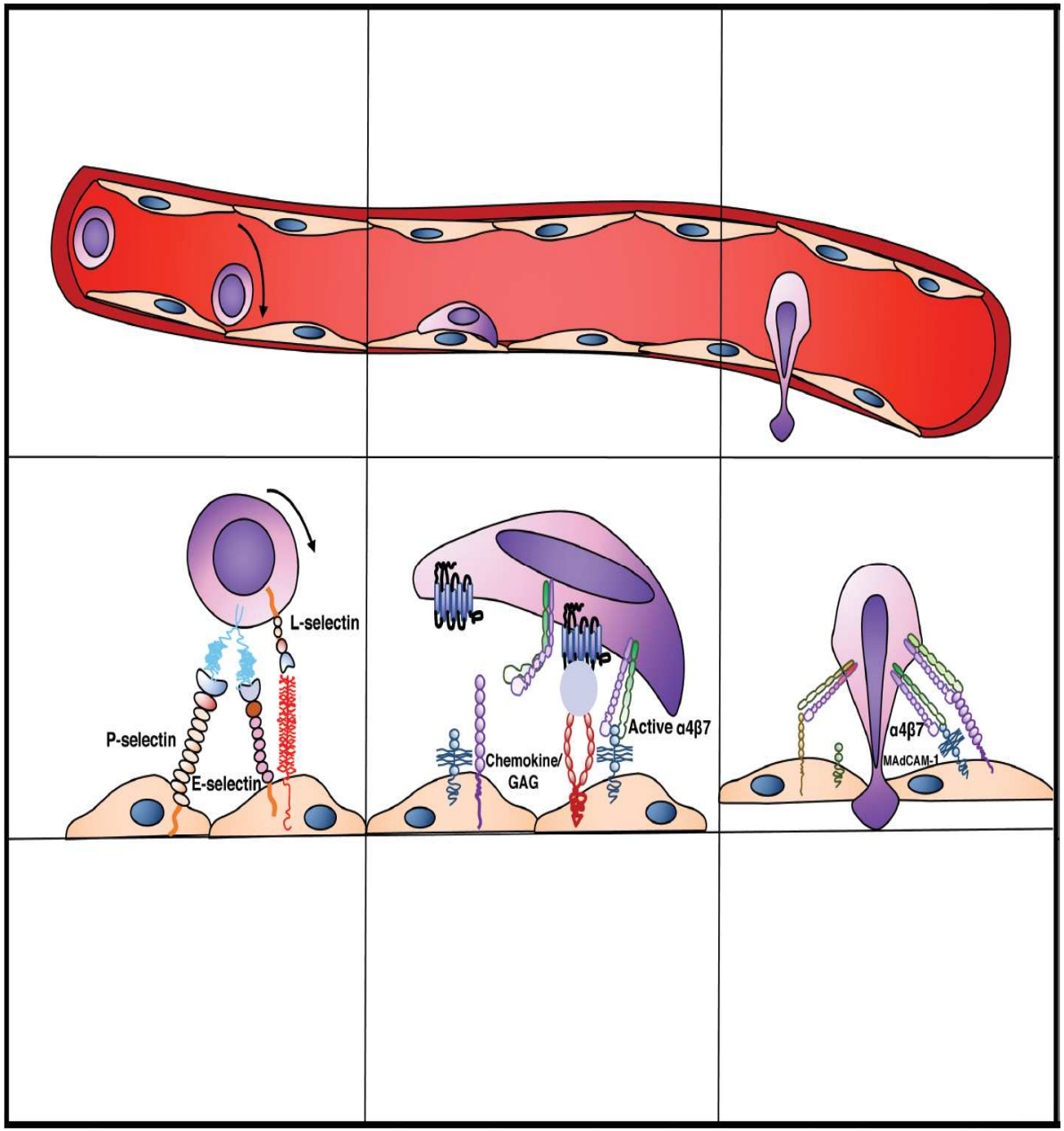


Ahluwalia A et al. Scand J Gastroenterol. 2018;53:379-389



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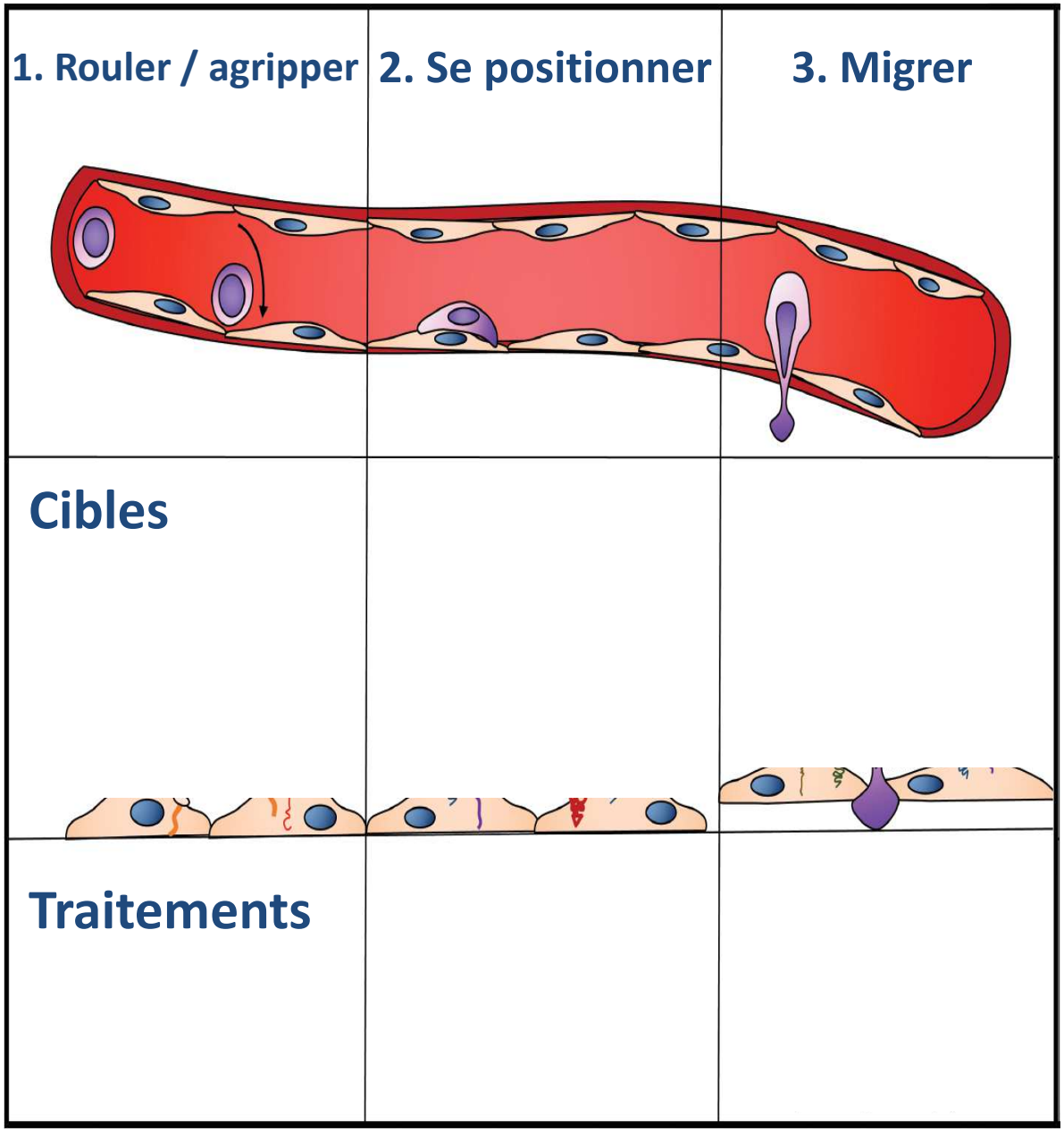
Inflammatory Bowel Diseases, Volume 25, Issue 2, 24 August 2018, Pages 270–282, https://doi.org/10.1093/ibd/izy269

Pérez-Jeldres T *et al. IBD* 2018; doi:10.1093/ibd/izy269



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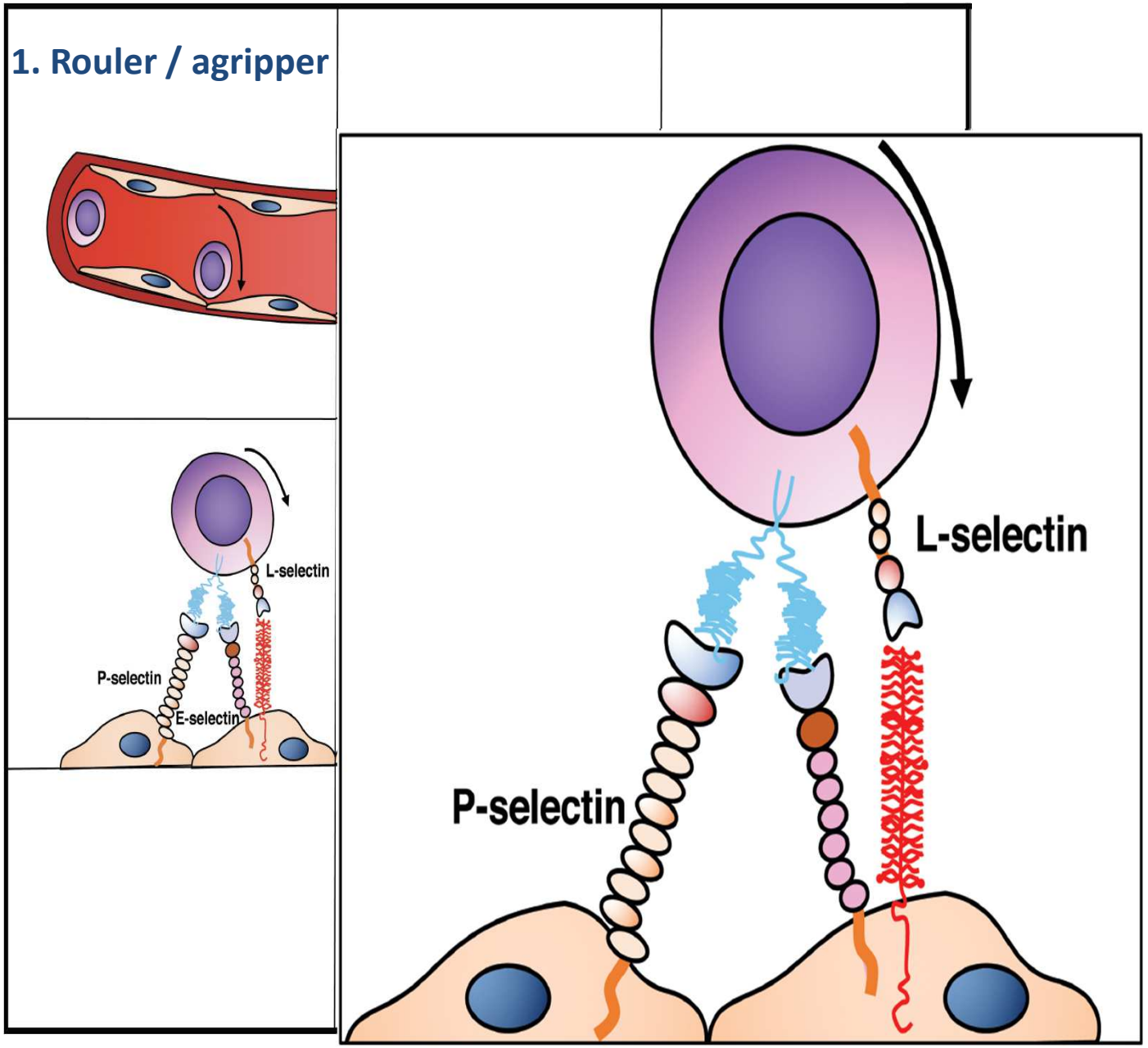
1. Rouler / agripper



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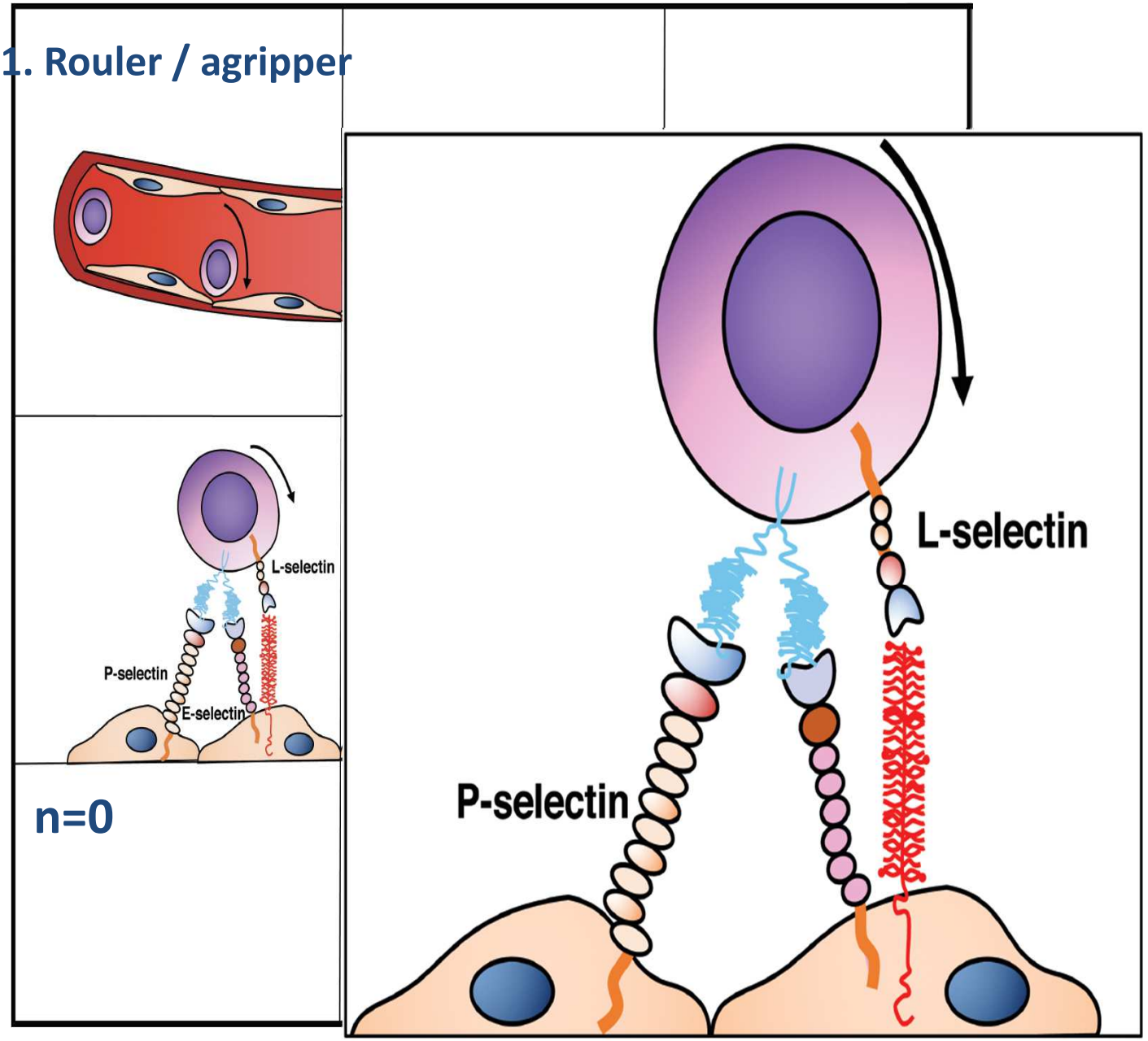

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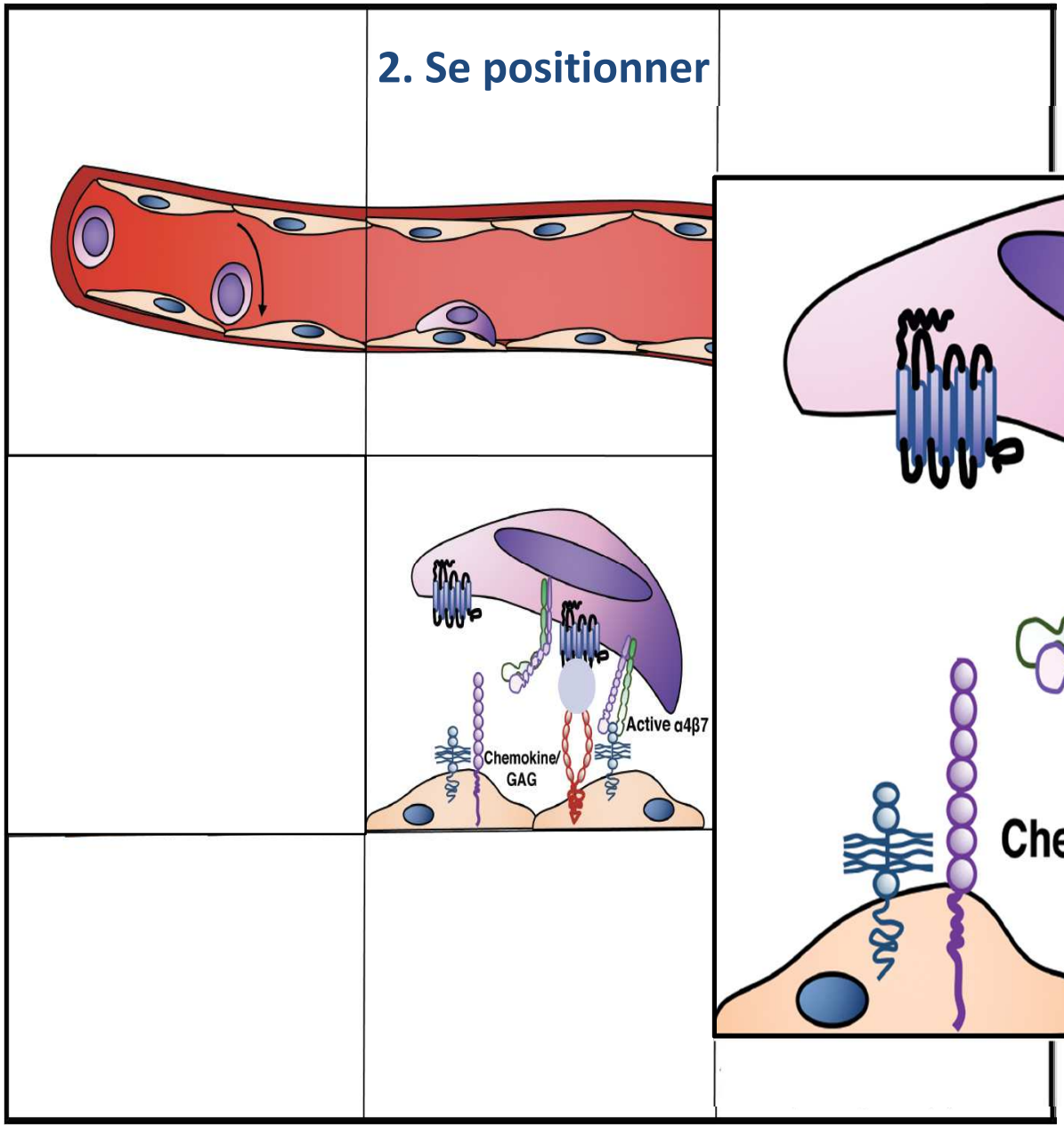
2. Se positionner



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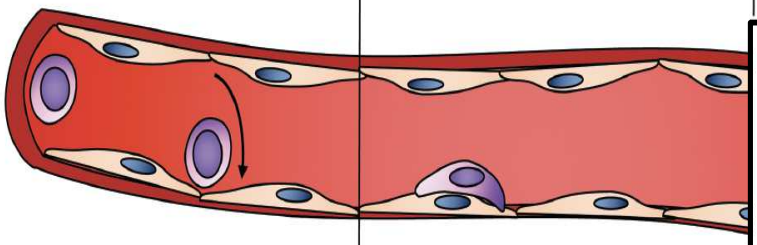
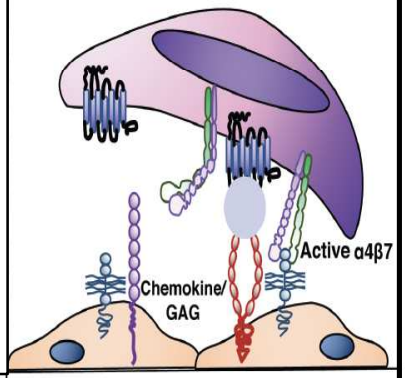
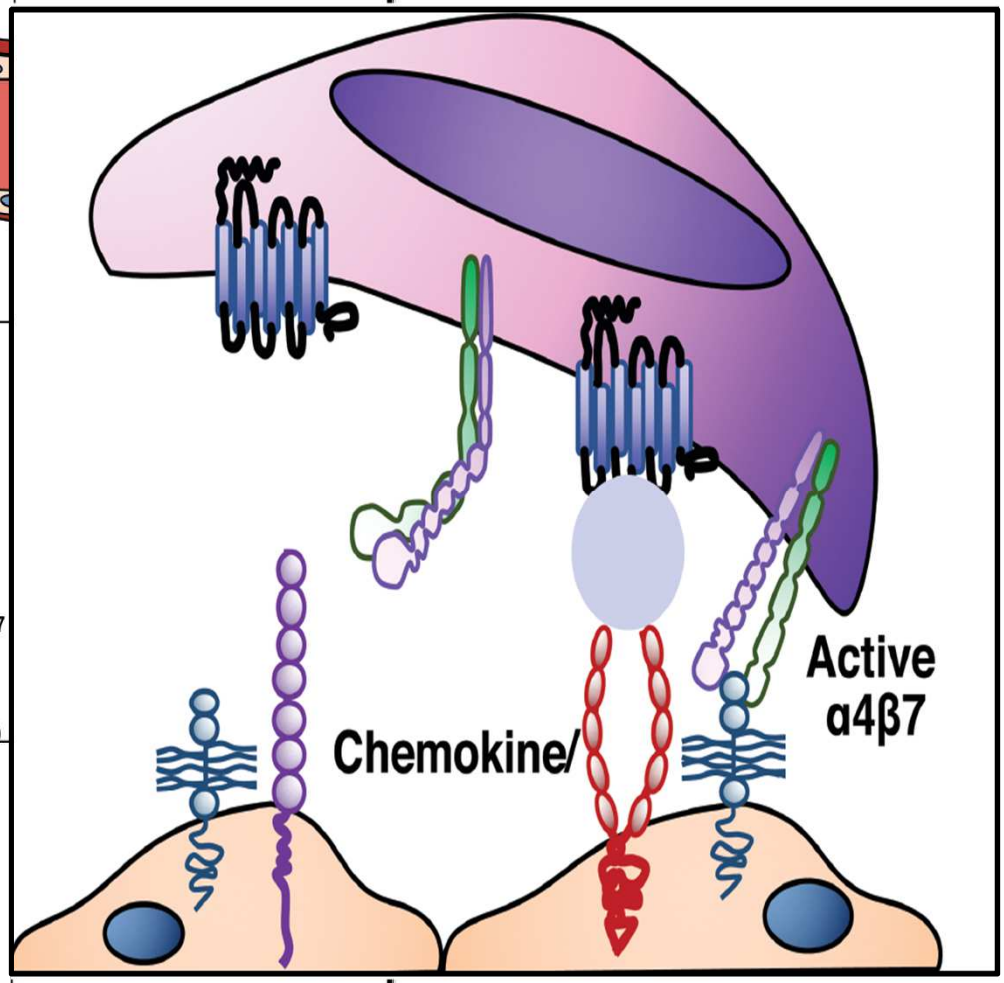




Vercinon (anti-CCR9)
Eldemumab (mAb anti-CXCL10)
GSK3050002 (mAb anti-CCL20)

n=3

(2 négatifs)



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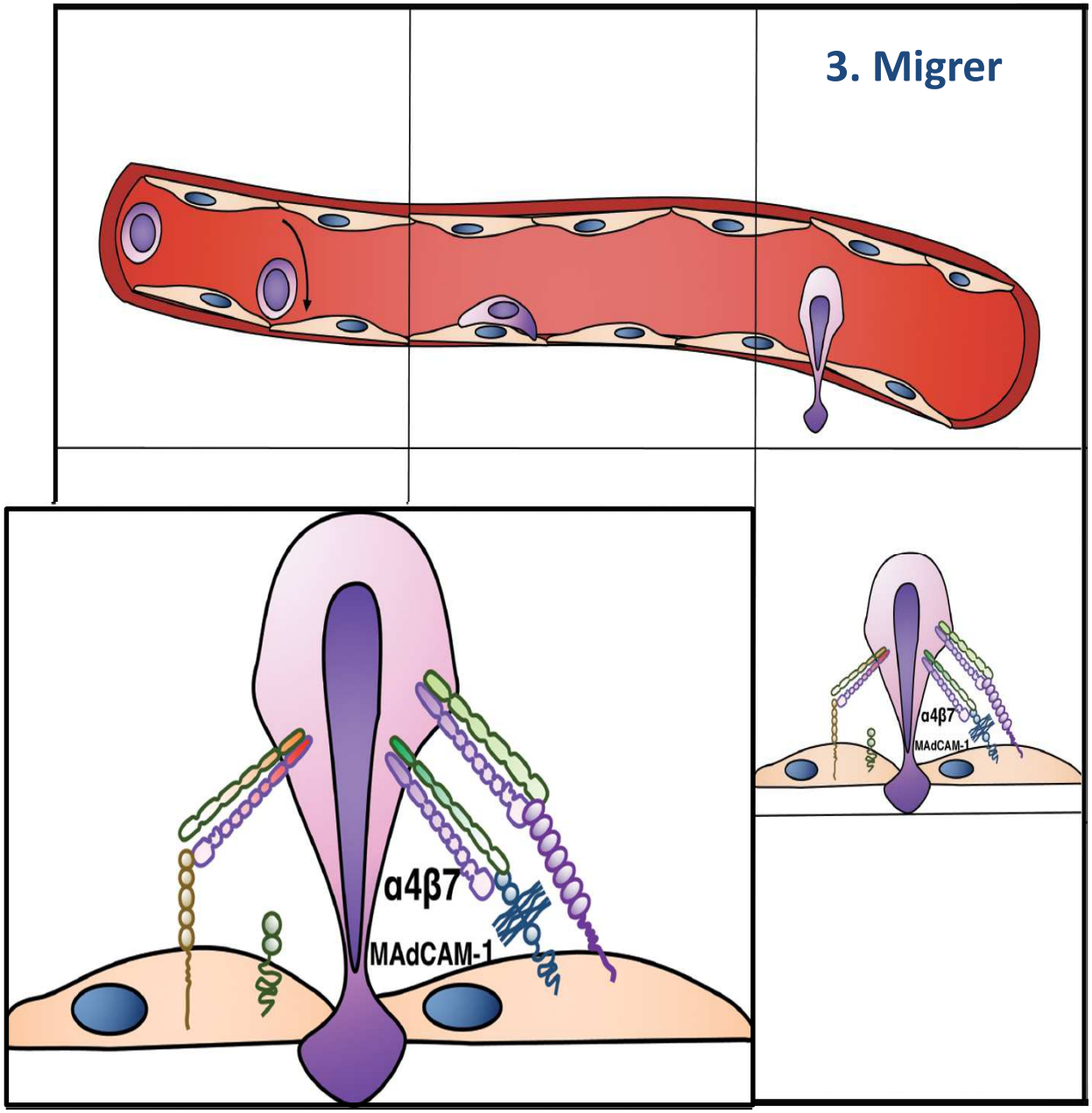

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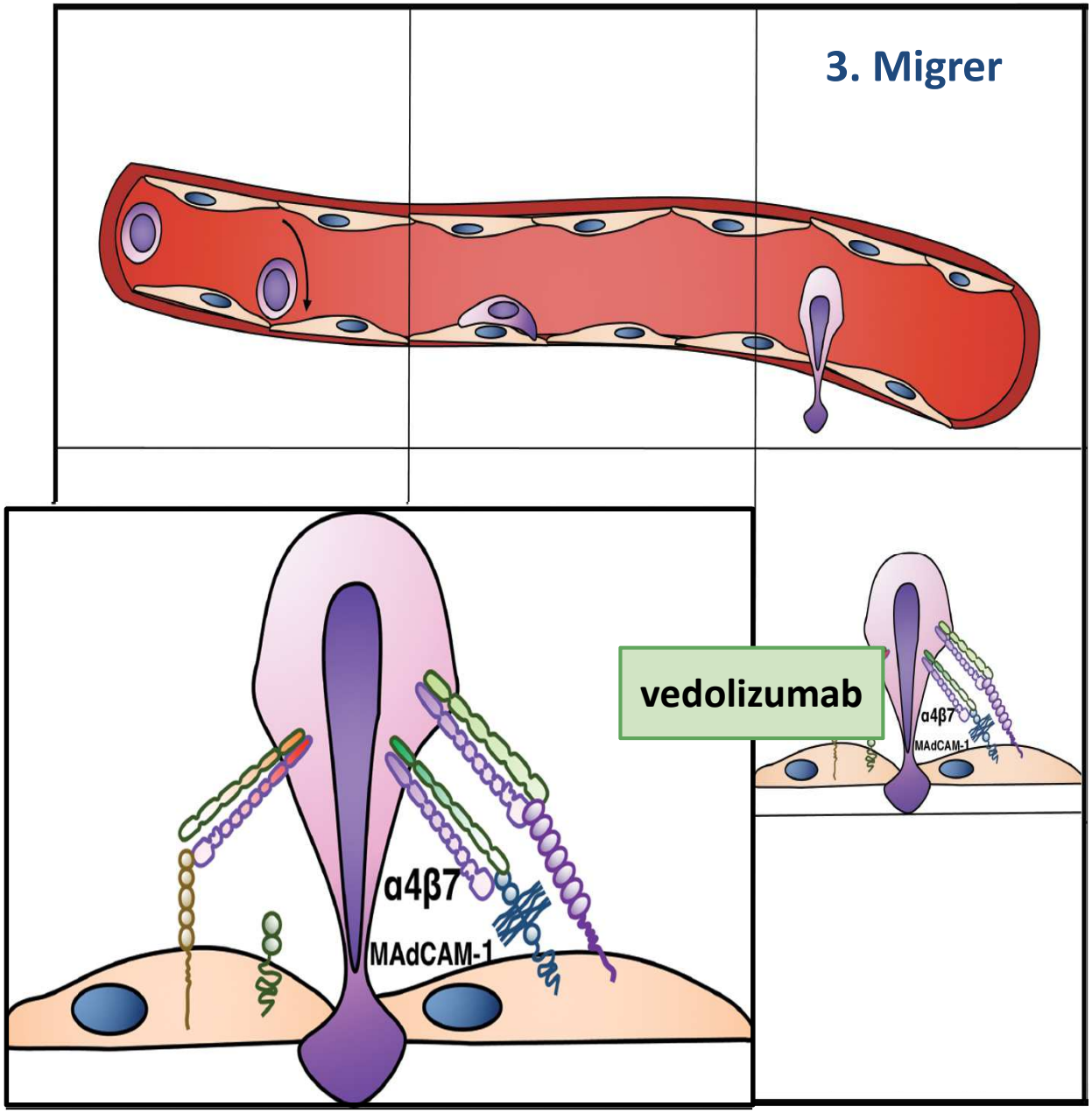

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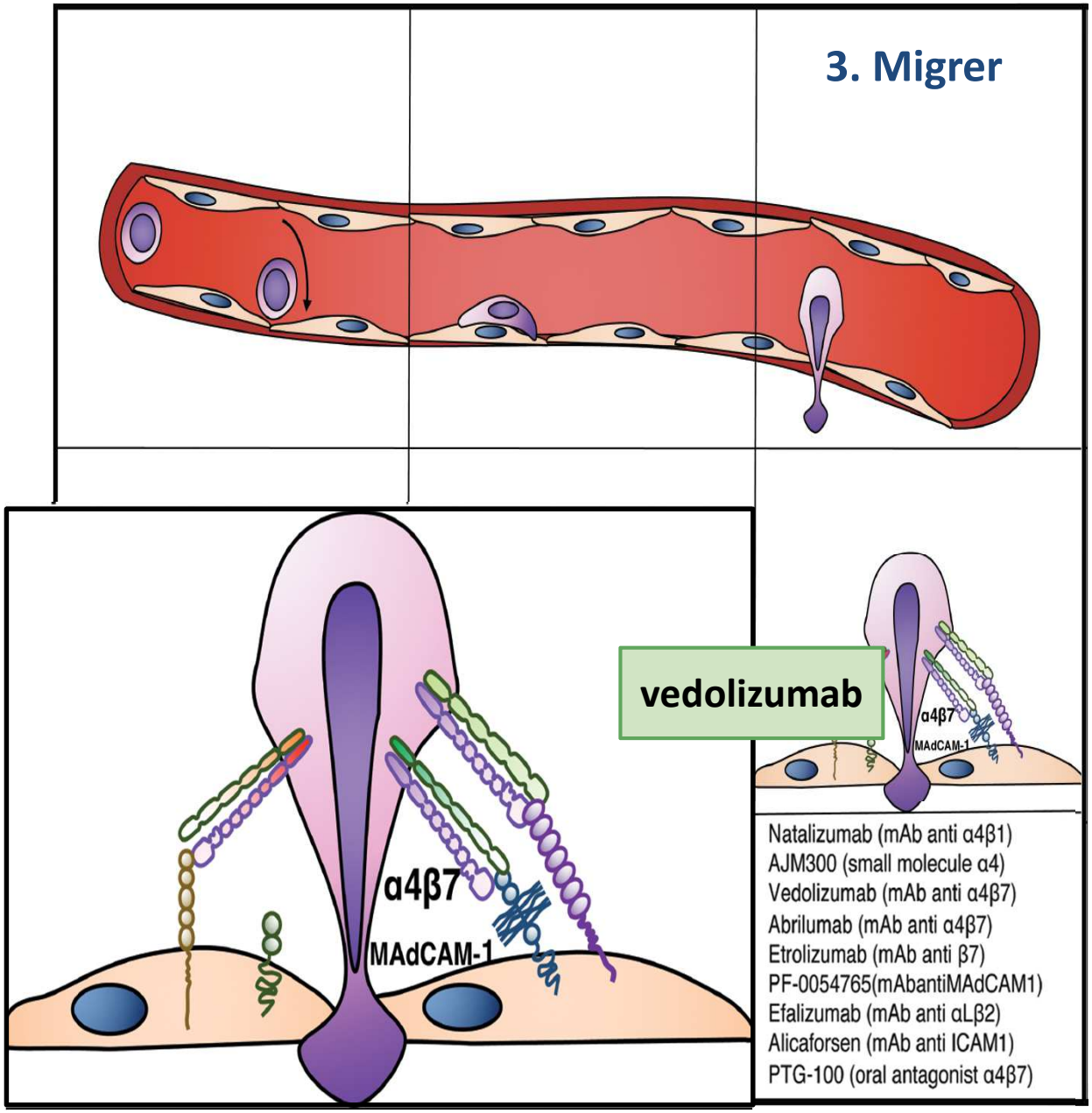

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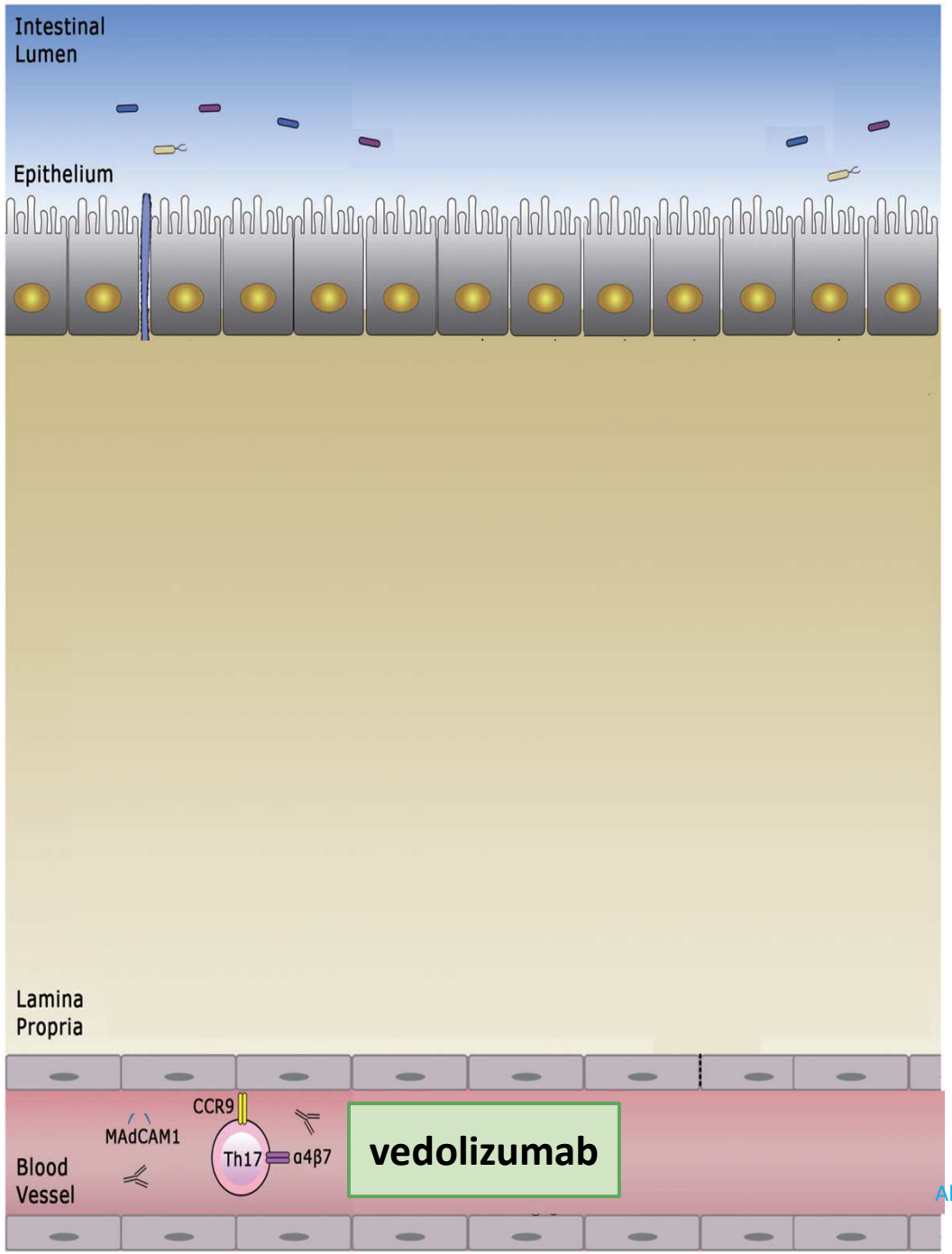
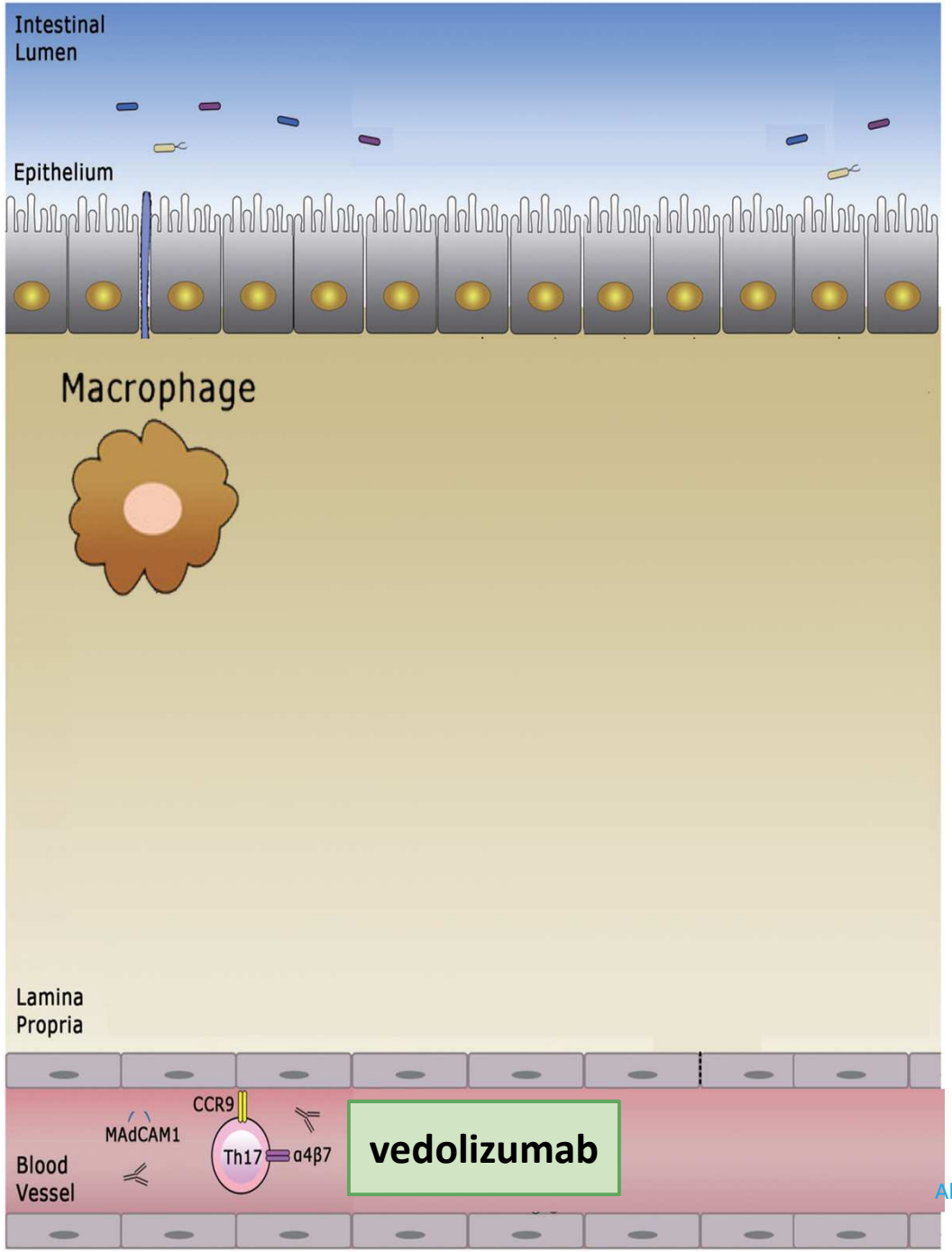
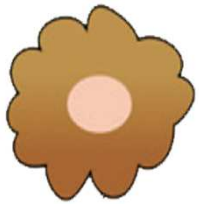


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.



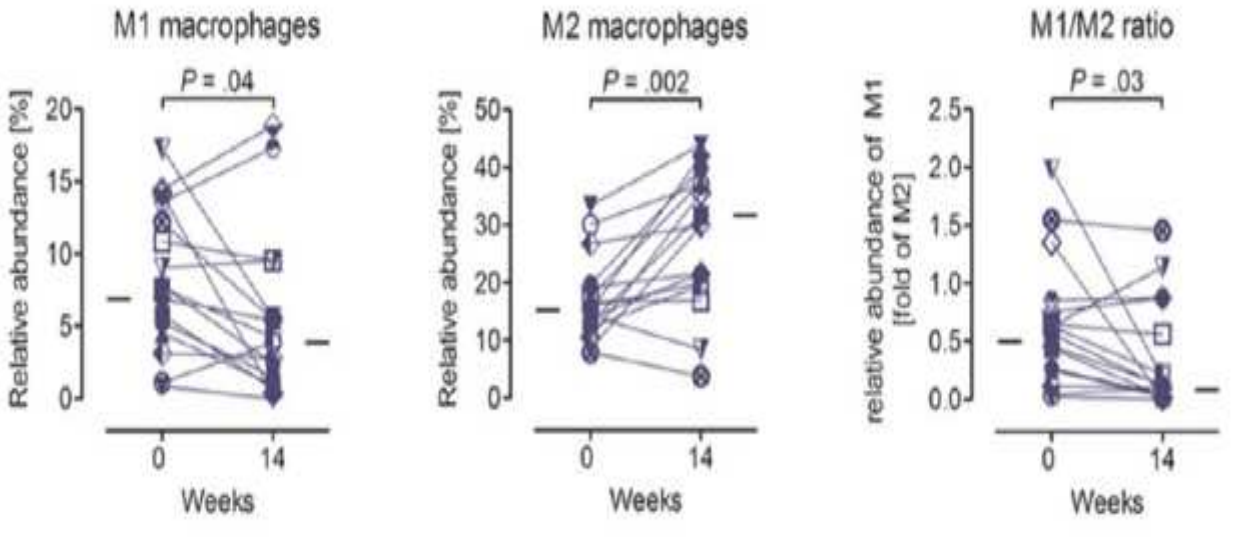
Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

Macrophage



vedolizumab

Immunité innée !!!



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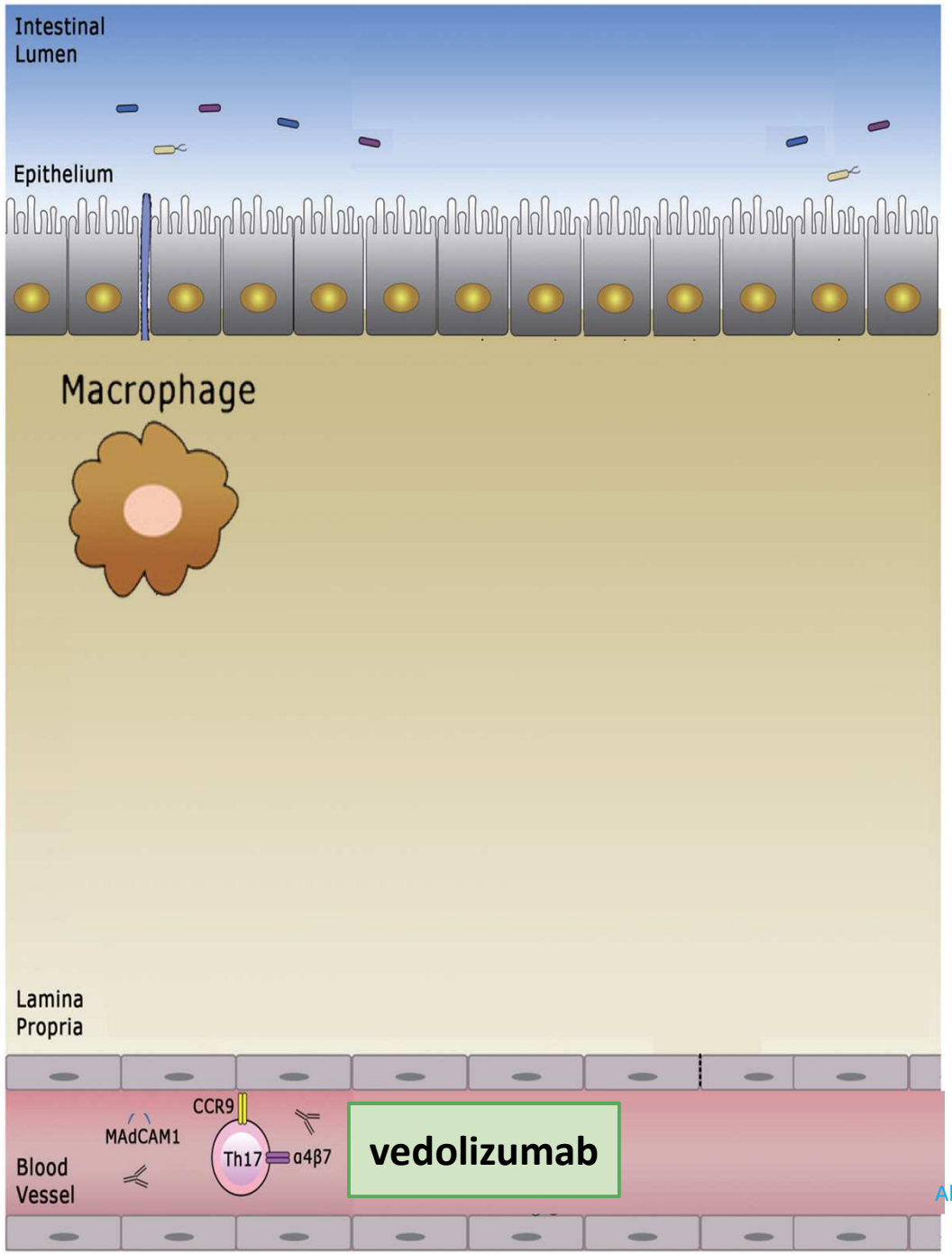
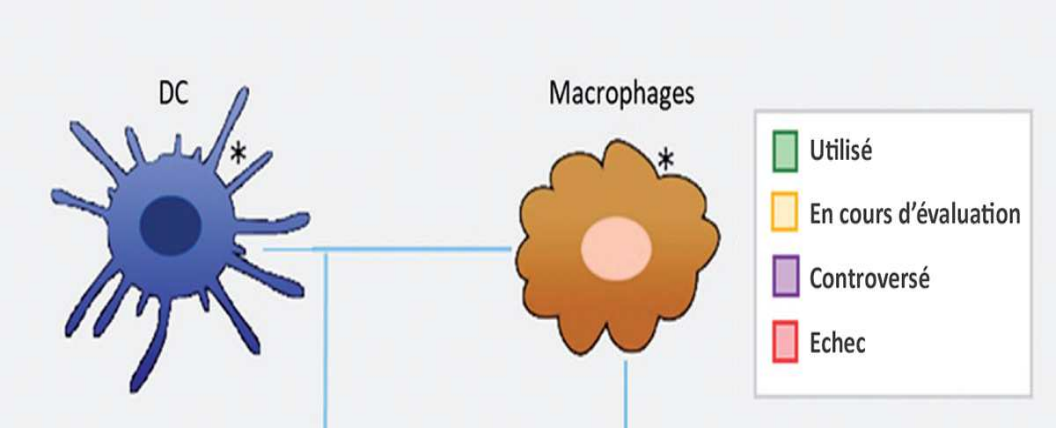


Ahluwalia A *et al. Scand J Gastroenterol.* 2018;53:379-389.

La fin du voyage



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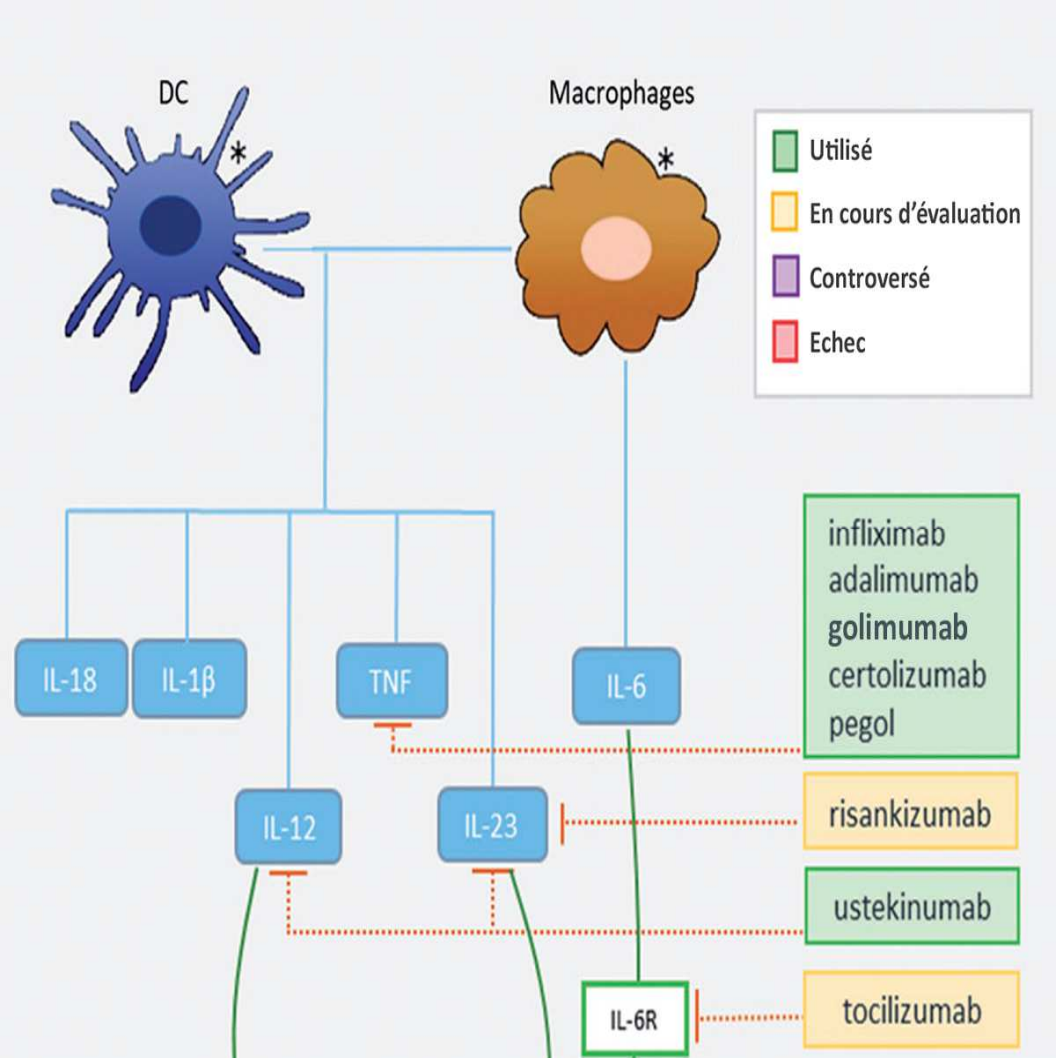
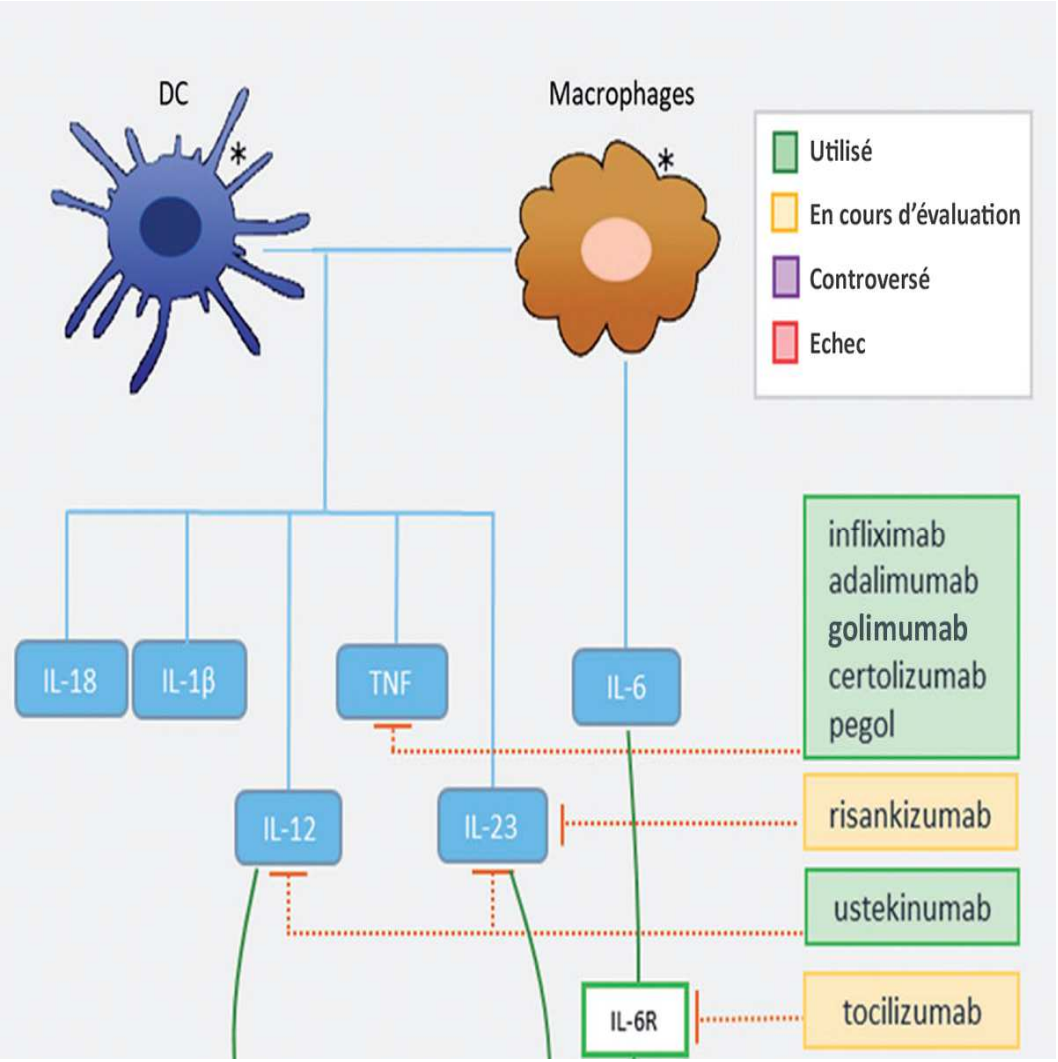

DC
Macrophages
Utilisé
En cours d'évaluation
Controversé
Echec
IL-18
IL-1β
TNF
IL-6
IL-12
IL-23
IL-6R
infliximab
adalimumab
golimumab
certolizumab
pegol
risankizumab
ustekinumab
tocilizumab

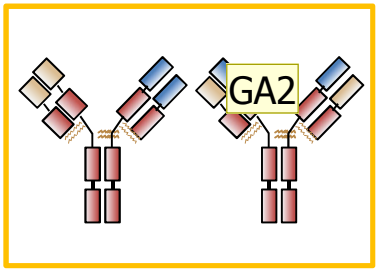
GA1

Diapositive 74

GA1 Golimumab

Gillet, Alexis; 13/03/2019



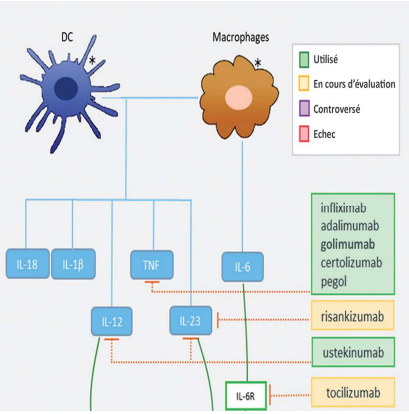


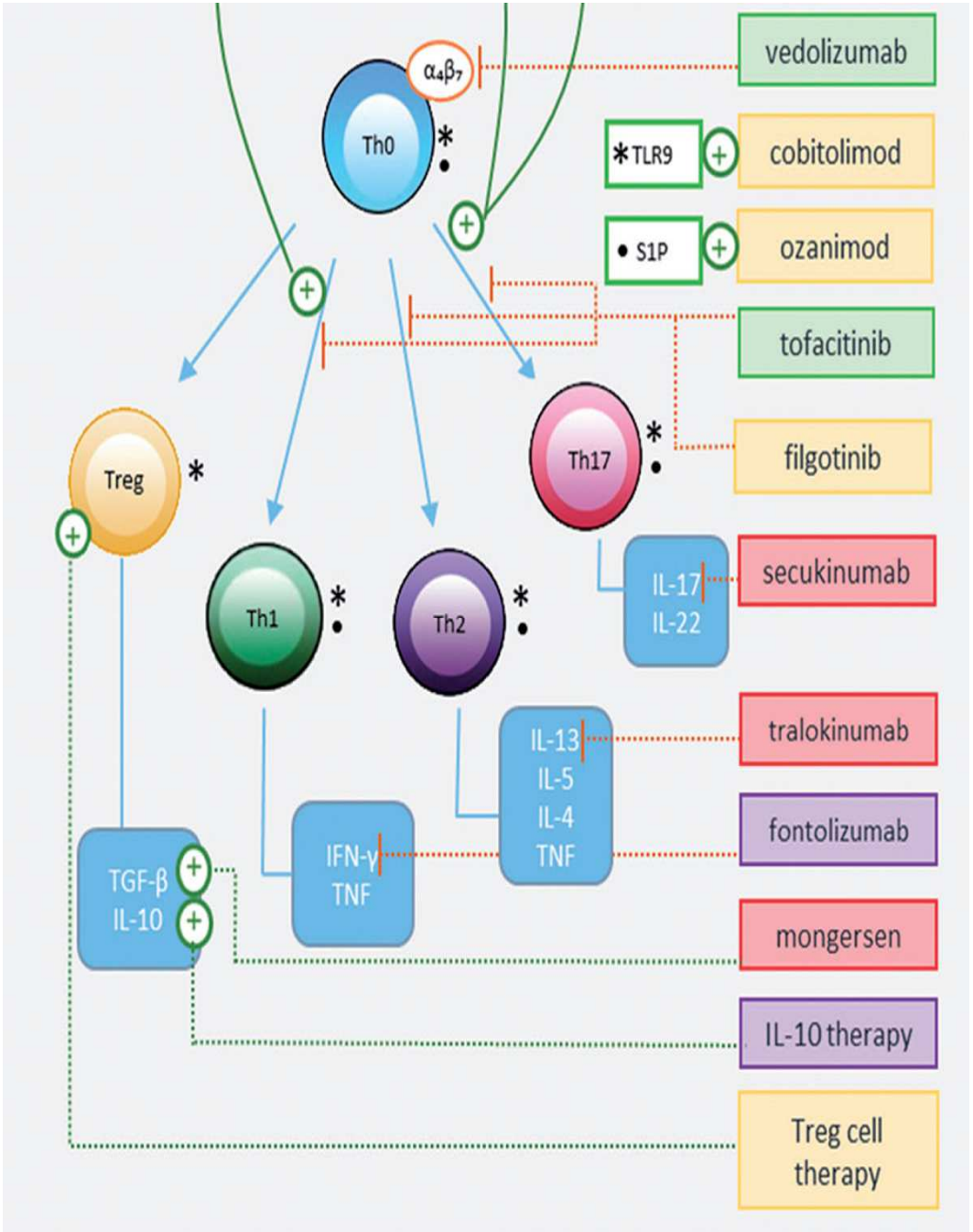
Brazikumab (MEDI 2070
mirizumab
guselkumab

Diapositive 75

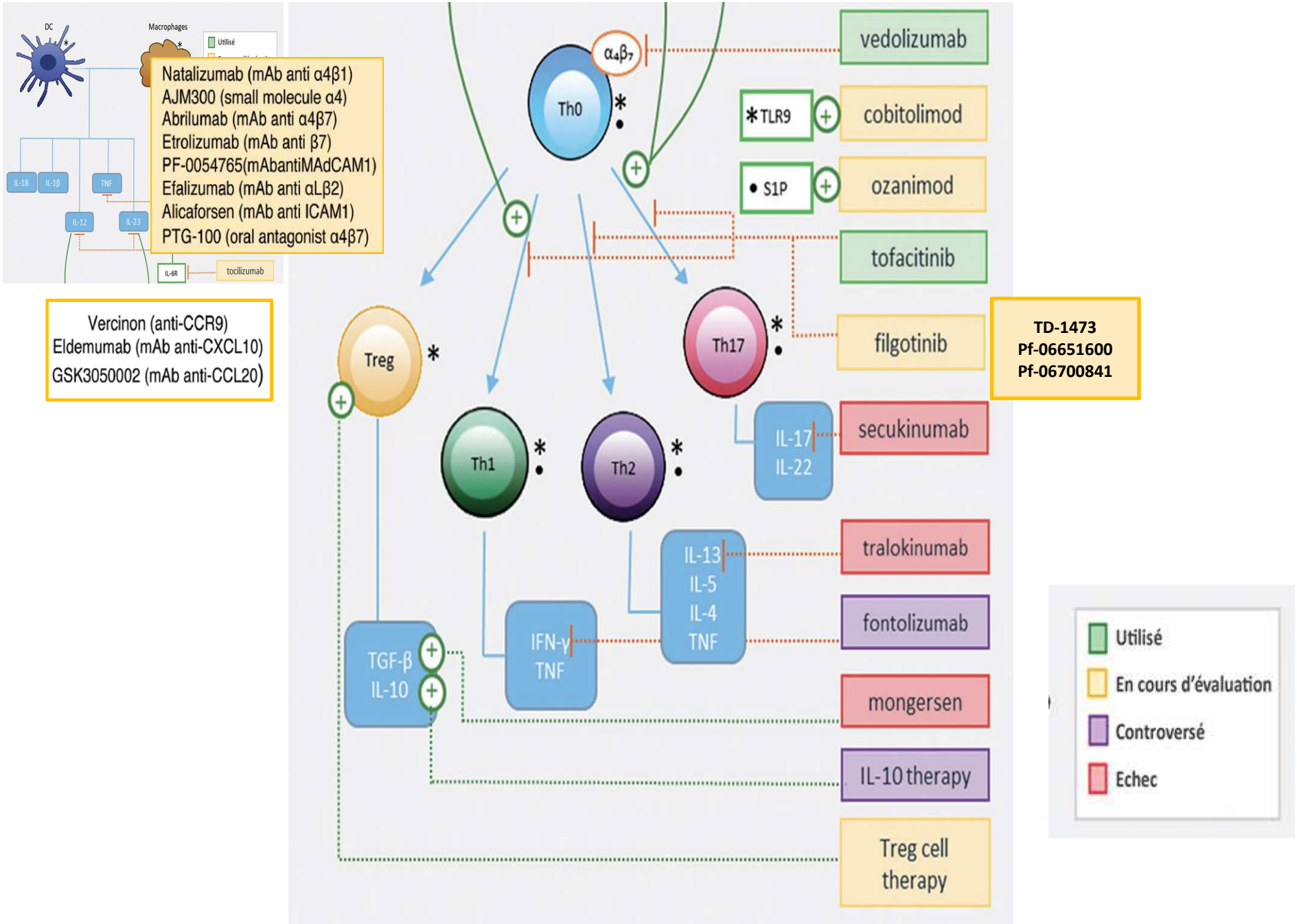
GA2 Golimumab

Gillet, Alexis; 13/03/2019


DC
Macrophages
Utilisé
En cours d'évaluation
Controversé
Echec
IL-18
IL-1β
TNF
IL-6
IL-12
IL-23
IL-6R
infliximab
adalimumab
golimumab
certolizumab
pegol
risankizumab
ustekinumab
tocilizumab


Th0
α4β7
vedolizumab
TLR9
cobitolimod
S1P
ozanimod
tofacitinib
Treg
Th17
filgotinib
Th1
Th2
IL-17
IL-22
secukinumab
IL-13
IL-5
IL-4
TNF
tralokinumab
IFN-γ
TNF
fontolizumab
TGF-β
IL-10
mongersen
IL-10 therapy
Treg cell therapy


Utilisé
En cours d'évaluation
Controversé
Echec


DC
Macrophages
Utilisé
IL-18
IL-1β
TNF
IL-12
IL-23
IL-6R
tocilizumab
Natalizumab (mAb anti α4β1)
AJM300 (small molecule α4)
Abrilumab (mAb anti α4β7)
Etrolizumab (mAb anti β7)
PF-0054765(mAbantiMAdCAM1)
Efalizumab (mAb anti αLβ2)
Alicaforsen (mAb anti ICAM1)
PTG-100 (oral antagonist α4β7)
Vercinon (anti-CCR9)
Eldemumab (mAb anti-CXCL10)
GSK3050002 (mAb anti-CCL20)
Th0
α4β7
vedolizumab
TLR9
cobitolimod
S1P
ozanimod
tofacitinib
Treg
Th17
filgotinib
TD-1473
Pf-06651600
Pf-06700841
Th1
Th2
IL-17
IL-22
secukinumab
IL-13
IL-5
IL-4
TNF
tralokinumab
IFN-γ
TNF
fontolizumab
TGF-β
IL-10
mongersen
IL-10 therapy
Treg cell therapy
Utilisé
En cours d'évaluation
Controversé
Echec

Soyons/SOYEZ enthousiastes !!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!

MERCI